Cerebrovascular diseases 2

P2001
MATRIX METALLOPROTEINASE-2-1575 G/A POLYMORPHISM AS A RISK FACTOR FOR ANEURYSMAL SUBARACHNOID HEMORRHAGE
A. Borratynska¹, A. Slowik¹, T. Dziedzic¹, J. Pera¹, A. Klimkowicz-Mrowiec¹, D. Wloch¹, R. Czepko², A. Szczudlik¹
¹Neurology Department, ²Neurosurgery Department, Jagiellonian University, Krakow, Poland

Background and aim: Data suggest that extracellular matrix remodelling plays a role in the pathogenesis of aneurysmal subarachnoid haemorrhage (SAH) in humans. The aim of the study was to assess the significance of matrix metalloproteinase-2 (MMP-2) –1575 G/A polymorphism as risk factor for aneurysmal SAH.

Material and methods: 239 patients with aneurysmal SAH (mean age: 50.0±12.6 years), and 241 healthy controls matched for age and sex, were genotyped for the MMP-2 G/A polymorphism. Aneurysmal SAH was diagnosed by cranial computed tomography, and/or lumbar puncture and digital subtraction angiography. Data concerning demographics and possible risk factors for SAH were collected. MMP-2 genotypes were determined by PCR and RFLP methods.

Results: The MMP-2 genotype distribution in patients with aneurysmal SAH (AA-3.0%, AG-39.3%, GG-57.7%) differed significantly from the controls (AA-7.9%, AG-39.0%, GG-53.1%) (p<0.001). A logistic regression model showed that the AA genotype (OR=0.69, 95%CI: 0.49–0.98), cigarette smoking, excessive alcohol consumption, and hypertension independently affected the risk for aneurysmal SAH.

Conclusion: The study shows for the first time that AA genotype of MMP-2 –1575 C/T polymorphism is associated with the reduced risk of aneurysmal SAH in a Polish population.

P2002
STROKES AND FETAL VARIANTS IN VERTEBROBASILAR TERRITORY
P. Cardona¹, L. Bau¹, M. Cos², A. Escrig¹, F. Rubio¹
¹Department of Neurology, Bellvitge Hospital, Barcelona, Spain, ²Department of Neuroradiology, IDI

The incidence of clinic and etiology in strokes of posterior cerebral artery (PCA) show a great heterogeneity. The contribution of the carotid territory to its affectation is unknown.

Patients and methods: We carry out a retrospective study of the patients with stroke in territory of PCA, who entered our centre between 2001–2005. We made a clinical analysis of risk factors, ultrasonography study, determination of vascular territory affected by magnetic resonance and prognosis.

Results: They represent 9% of the strokes (113 patients). The etiology was in 40% indeterminate, 33% cardioembolic and 27% atherothrombotic. The clinical affectation in scale NIH is worse in those of atherothrombotic etiology (p<0.05). Visual alterations were most frequent (82%), followed by motor (56%). In the vascular study, 22% of them show significant carotid stenosis and 17% the fatal variant of ACP; these findings were associated with severe clinical affectation (p<0.005). With regard to the prognosis, the mortality was 3% and recurrence 5%.

Discussion: The descriptive analysis highlights the presence in half of cases of hemiparesis, hemihypoesthesia and hemianopsia, characteristic of the affectation of the middle cerebral artery. In our series 17% of PCA strokes showed the persistence of fetal circulation (P1 agenesia), and the great majority associated important haemodynamic affectation of the carotid that irrigated it, in relation to severe carotid stenosis.

Conclusion: The etiology of the PCA strokes in the majority of cases is indeterminate. The presence of anatomic variant of PCA and its association with severe carotid stenosis is related, with worse clinical affectation and prognosis.

P2003
CLINICAL SIGNIFICANCE OF MICROEMBOLISM IN ACUTE ISCHEMIC STROKE
Department of Neurology, Yeungnam University School of Medicine, Daegu, South Korea

Background: Microembolic signals (MES) detected by transcranial Doppler (TCD) have been considered as an independent predictor of recurrent ischemic stroke. However, the association between the presence of MES and the risk of stroke has predominantly been studied on a small and selected group of patients. To evaluate the clinical significance of MES in patients with acute ischemic stroke, we investigated the prevalence of MES and analyzed the relationship between MES and stroke subtype. Methods: We intended to perform TCD monitoring to detect MES from the bilateral middle cerebral arteries in patients within 15 days of stroke onset. The strokes were subtyped using the TOAST classification criteria.

Results: TCD study was performed on 500 consecutive ischemic stroke patients who were admitted to our stroke unit within 7 days of stroke onset and 65 were excluded because there was a long interval between onset of symptoms and examination, an artificial heart valve, and inadequate temporal bone window. MES were detected in 23 (4.2%) despite the fact that all patients were receiving an antiplatelet or anticoagulant treatment. MES were detected in 23 (4.2%) despite the fact that all patients were receiving an antiplatelet or anticoagulant treatment. MES were detected in 3.1% of patients with large-artery atherosclerosis stroke, 4.1% of cardioembolic stroke, 2.1% of lacunar stroke, 9.1% of cryptogenic stroke, and 4.1% of undetermined stroke (p=0.241). In 6 of the 8 patients (75%) with the anterior circulation infarct, MES were observed ipsilateral to the affected territories.

Discussion: During antithrombotic treatment, the prevalence of MES is low and MES detection dose not improve ischemic stroke subtype classification. The MES are frequent in the territories of symptomatic arteries in the anterior circulation stroke.
P2004
THE EFFECTS OF A RECOMBINANT HUMAN COAGULATION FACTOR VII, NOVOSEVEN 50 UG/KG IN PATIENTS WITH INTRACEREBRAL HEMORRHAGE: A CASE SERIES
A. Ehtisham1, S. Taylor2, M.W. Klein3
1Neurocritical Care Unit, Via Christi Regional Medical Centre, 2Departments of Neurology and Neurosciences, University of Kansas School of Medicine at Wichita, 3Department of Pharmacy, Wichita, KS, USA

Introduction: Intracerebral haemorrhage is associated with high incidence of morbidity and mortality, and resultant cerebral oedema is of particular concern. An ideal treatment would halt haematoma expansion without thromboembolic events. Early studies in intracerebral haemorrhage have shown promise in NovoSeven, a recombinant factor VII. However, the ideal dose and timeframe of NovoSeven is unidentified. We report our results with NovoSeven in the management of 10 patients with intracerebral haemorrhage.

Methods: Patients with low risk for thromboembolic events were eligible for NovoSeven therapy. A NovoSeven dosing of 50 ug/kg was used at various timeframes post symptom-onset.

Results: 8 of 10 patients (80%) survived their hospital stay. Average length of hospital stay was 3.3 days (S.D. ± 4.3 days). 4 of 10 patients (40.0%) received NovoSeven less than 8 hours after symptom onset, 3 patients (30.0%) between 4 and 8 hours after symptom onset and the remaining 3 patients (30.0%) over 8 hours after symptom onset. Average baseline haemorrhage volume was 26.92 cm³ (S.D. ± 18.57 cm³) and 26.80 cm³ (S.D. ± 17.02 cm³) post-NovoSeven. Average percent change in haemorrhage volume was an increase of 6.3% (S.D. ± 33.1%). Treatment failure (≥30% increase in haemorrhage volume) occurred in 2 of 10 patients (20.0%). No thromboembolic events occurred in any patients.

Conclusions: These results suggest NovoSeven at 50 ug/kg may be safe and effective for haemostasis at various timeframes in selected patients with intracerebral haemorrhage.

P2007
LOCALIZATION OF PURE SENSORY STROKE
C.K. Ha, K.H. Ji, S.R. Kim, J.H. Rha
Department of Neurology, Inha University Hospital, Inchon, South Korea

Background and aims: Anatomical substrate of pure sensory stroke (PSS) is widely known as thalamic lesion. However non-thalamic, especially pontine lesion, also may produce PSS. We evaluate the frequency of PSS caused by extrathalamic lesion.

Methods: We studied 2142 consecutive patients with acute ischemic stroke, hospitalized within seven days after onset, from Inha Stroke Registry between January 2002 and September 2006. Brain MRI was performed in all cases. As PSS was determined by presenting symptoms and signs, evolving cases from sensory motor to pure sensory symptom were discarded. We also excluded TIA cases without corresponding lesion in MRI, but cerebral infarctions with transient symptoms were included.

Results: 49 patients were identified to have PSS (32 men, 17 women, age 42-78). Most of them (31, 61%) had a thalamic infarction. 10 patients (20%) had a pontine, and 5 (10%) had a medullary infarction. The remaining 4 patients had infarction at corona radiata, anterior choroidal artery territory, PCA territory (thalamus and occipital lobe), and posterior limb of internal capsule, respectively. In 4 of 10 pontine infarction patients, sensory symptoms were confined to the acral part of body (1 at finger tip, 2 at hand, and 1 at hand and foot).

Conclusion: Our result support PSS, especially when confined to acral part, is frequently associated with brainstem lesion.

P2008
PRELIMINARY SCREENING RESULTS FOR FABRY DISEASE IN YOUNG STROKE PATIENTS REVEALS A NEW MUTATION
C.M. Hemelaer1, B. Poppe2, A. Sieben1, F. Vanhee1, P. Proot1, M. De Clerck1, B.P. Leroy1, J.F. De Backer1, B. Wuys1, L.J. De Meirleir1, J.L. De Reuck1
1Department of Neurology, 2Department of Medical Genetics, 3Department of Ophthalmology, 4Department of Cardiology, 5Department of Clinical Chemistry, 6Department of Metabolic Diseases, Ghent University Hospital, Ghent, Belgium
Introduction: Fabry disease is an X-linked recessive lysosomal storage disorder with multiorgan involvement due to accumulation of glycosphingolipids, as a result of α-galactosidase deficiency caused by mutations in the GLA gene at Xq22. Clinical symptoms include acroparesthesias, angiokeratoma, hypohidrosis, cardiac and renal failure, cornea verticillata and stroke.

Methods: Between September 2005 and January 2007, 119 consecutive young patients (54 f, 65 d, <60 years) with stroke or unexplained white matter lesions were screened biochemically and genetically for Fabry disease. Male patients were screened for α-galactosidase activity. When activity was nearly absent, genetic analysis was performed. Due to random X chromosome activation heterozygote females can have normal α-galactosidase activity, so mutation analysis was performed in the case of all female patients.

Results: Mutation analysis revealed polymorphisms of the GLA gene in 6 women. One 20-year-old male Fabry patient was identified. He had no history of typical symptoms or signs. He presented with a febrile syndrome with meningeal irritation, pain in the right arm, and vertebrobasilar TIA. Further investigations revealed cornea verticillata and retinal arterial tortuosity, microalbuminuria, and cardiac hypertrophy. Genetic analysis revealed a new missense mutation (c.75K=C; p.Ile253Thr).

Conclusions: Stroke can be the presenting symptom of Fabry disease, even in young patients. Screening for Fabry disease should be part of the diagnostic evaluation in young stroke patients. Our preliminary results show a lower frequency (0.8%) of Fabry disease compared to recent data from a German cohort with cryptogenic stroke (2.4–4.9%). Male Fabry patients may present with atypical symptoms without a history of classical signs.

P2009
S-100B PROTEIN AS A PREDICTOR OF THE EARLY RECANALIZATION OF THE ACUTE MIDDLE CEREBRAL ARTERY OCCLUSION
R. Herzig1, P. Schneiderka1, S. Burval1, D. Sanak1, I. Vlachova1, D. Skoloudik1, M. Kral1, J. Zapletalova4, A. Bartkova1, J. Mares1, M. Herman1, P. Kanovsky1
1Department of Neurology, Faculty of Medicine and Dentistry, Palacký University and University Hospital, 2Department of Clinical Biochemistry, University Hospital, 3Department of Radiology, Faculty of Medicine and Dentistry, Palacky University and University Hospital, 4Institute of Biophysics, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic

Background and aims: S-100B protein (S-100B) is an acidic calcium-binding protein found in the nervous system of vertebrates, where it is released by damaged brain tissue. The aim was to assess its role as a predictor of the early recanalization (<6 hours since symptoms onset) in acute proximal middle cerebral artery (MCA/M1) occlusion.

Methods: A prospective, hospital-based study was used. The set of 40 patients (22 males, 18 females; aged 25–81, mean 65±11.5 years), presenting with acute stroke due to MCA/M1 occlusion on magnetic resonance angiography (MRA). Serum S-100B levels were measured 24, 48, 72, 96 hours following the onset of cerebral infarction. MCA recanalization was assessed using transcranial Doppler sonography and MRA. Mann-Whitney test was applied when assessing the relationship between the particular and also maximal S-100B values and MCA recanalization.

Results: The following S-100B values (ug/l) were significantly lower in patients with early MCA recanalization when compared to those without recanalization – S-100B48 (mean 0.313 versus 1.459, p=0.008), S-100B72 (mean 0.235 versus 1.195, p=0.001), S-100B96 (mean 0.204 versus 0.967, p<0.001) and S-100Bmax (mean 0.320 versus 1.847, p<0.0003). Also S-100B24 values were lower in patients with MCA recanalization; however, this difference was not statistically significant.

Conclusions: Serum S-100B values measured at 48, 72 and 96 hours, as well as the maximum S-100B value obtained within the 24-96 hour interval following the MCA/M1 occlusion can be used as a prognostic marker of the early (<6 hours) MCA/M1 recanalization. Acknowledgement: Supported by the IGA MH CR grant number NR/8579-3/2005.
ion. Cut-off values for normal IMT were used according to the criteria set by Salonen and Salonen (Atherosclerosis 1990).

**Results:** 147 patients (35.3%) had normal IMT values, and 270 patients (64.7%) were with pathological IMT. The following risk factors were registered in the total group of patients: 65.5% with hypertension, 49.5% with hypercholesteremia, 23.9% with diabetes and 18.5% with smoking. The correlation between pathological IMT and hypertension was statistically significant (p<0.0001), as well as the correlation between pathological IMT and diabetes (p<0.001). Hypercholesteremia was also reliably correlated to pathological IMT (p<0.05), while smoking had no significant correlation to IMT. Patients with normal IMT had a lower burden of 4 above mentioned risk factors (mean 1.2) than those patients with pathological IMT (mean 1.8).

**Conclusion:** Pathological IMT of carotid arteries was a good indicator for arteriosclerotic process in our patients with major modifiable risk factor for arteriosclerosis (hypertension, diabetes and hypercholesteremia), except for those with smoking habits.

**P2012**

A SIMPLE AND RAPID SCALE CAN DETECT THROMBOLYSIS CANDIDATES

H.Y. Park, J.Y. Choi, T.S. Lim, J.H. Yoon, H.S. Nam
Ajou University School of Medicine, Suwon, South Korea

**Background:** To detect thrombolysis candidates, rapid and accurate triage is of paramount importance. Although National Institutes of Health Stroke Scale (NIHSS) is widely used, it remains a complex scoring system necessitating training. Recently, the 3-Item Stroke Scale (3-ISS) has been reported as an excellent tool for predicting middle cerebral artery occlusion. We evaluated the hypothesis that the 3-ISS is feasible to detect thrombolysis candidates in the emergency department (ED) physicians.

**Methods:** The 3-ISS assessed three parameters: (1) level of consciousness, (2) gaze, and (3) motor function. Each item was graded 0 to 2, where 0 indicated normal findings and 2 severe abnormalities. In the ED, consecutive patients with stroke symptoms were prospectively collected during 3 months. An ED physician performed 3-ISS to each stroke patient, and a neurologist blindly checked NIHSS scores of the same patients within 30 minutes. The patients with more than 5 score in the NIHSS were regarded as potential thrombolysis candidates.

**Results:** 28 consecutive patients were enrolled during study periods. Among them, 16 (57%) patients were revealed as having had a stroke [ischemic stroke 10 (36%), hemorrhagic stroke 6 (21%)]. A strong correlation between 3-ISS and NIHSS scores was noted (r=0.73, p=0.00007). The points of 2 in the 3-ISS showed high sensitivity (100%) and specificity (66.7%) for predicting NIHSS score ≥5 in the Receiver Operating Characteristic (ROC) curve analysis.

**Conclusions:** The 3-item stroke scales were well correlated with NIHSS scores. In the emergency room, ED physicians or nurses might use this scale for rapid triage.

**P2013**

AUTO-EXPANDABLE STENTS IN THE MANAGEMENT OF INTRACRANIAL ANEURYSMS

R. Rangel Guerra1, A. Garcia De La Fuente2
1Centro de Especialidades Medicas, Monterrey, 2Hospital Christus Muguerza, Nuevo Leon, Mexico

**Introduction:** To present our experience in the treatment of Intracranial aneurysms using autoexpandable stents.

**Material and methods:** From June 2001 to June 2005 34 patients were treated. Ages between 18 and 78 years old. There were 7 men and 27 women.

**Results:** 26 aneurysms were wide neck saccular aneurysms and 8 were fusiform aneurysms. 8 were small, 13 median, 6 large and 7 giant. 6 were cavernous, 5 ophthalmic, 7 posterior communicating, 3 chorioidal, 3 in the carotid bifurcation, 3 in M1-M2 junction, 2 in the anterior communicating artery, 3 in V4, (two in the basal tip and one in P2 segment). A total of 40 stents were placed. 2 balloon expandable and 38 auto expandable were used. Bleeding during the procedure was observed in 4 patients, 5 patients died. In follow-up 27 patients were asymptomatic and 2 had disabling symptoms.

**Discussion:** In experimental studies stents have been shown to reduce the vorticity within the aneurysm stasis after stenting has been related to clinical improvement.

**Conclusions:** Stents are a good tool to preserve parent vessel in the treatment of difficult intracranial aneurysms and they have changed the conventional approach.

**P2014**

COLD SEASON INCREASES THE RISK FOR INTRACEREBRAL HEMORRHAGE IN SUBJECTS WITH UNTREATED HYPERTENSION

P. Saloheimo1, S. Tetri2, S. Juvela3, J. Pyhtinen1, M. Hillbom2
1Department of Neurology, 2Department of Neurosurgery, Oulu University Hospital, Oulu, 3Department of Neurosurgery, Helsinki University Central Hospital, Helsinki, 4Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland

**Background and aims:** Studies of the seasonal variation in the incidence of intracerebral haemorrhage (ICH) have resulted in conflicting findings. We investigated the role of ambient temperature in association with the known risk factors for ICH in a population-based cohort of patients with ICH.

**Methods:** Our study included all subjects with spontaneous ICH during a period of 3 years in Northern Ostrobothnia, Finland. The subjects were identified, and their clinical characteristics and outcomes were checked from hospital records and death records. The associations of the risk factors for ICH with ambient temperature were analyzed.

**Results:** We found 217 cases of incident ICH during the study period. 107 cases occurred during the warm period of the year (May to October) and 110 cases during the cold period (November to April). Subjects with untreated hypertension were significantly more frequently stricken of ICH during the cold than the warm period (p=0.018). In multivariate analysis, untreated hypertension was associated with an almost 3-fold risk for ICH during the cold period (OR, 2.87; 95% CI, 1.21–6.80; p=0.017). Furthermore, the admission blood glucose levels of ICH patients were lower during the cold than the warm period (p=0.023).

**Conclusions:** The increased risk for ICH during the cold season seems to be confined to those with untreated hypertension. This supports the hypothesis that the effect of ambient temperature on the risk of ICH is mediated by changes in blood pressure. Appropriate treatment of hypertension might prevent cases of ICH induced by cold.
P2015

DOES CLINICAL-DIFFUSION MISMATCH PREDICT GOOD CLINICAL OUTCOME IN ACUTE STROKE PATIENTS TREATED BY INTRAVENOUS THROMBOLYSIS?

D. Sanak1, A. Bartkova1, D. Horak1, R. Herzig1, I. Vlachova1, J. Zapletalova1, S. Burval1, J. Bucil2, M. Kral1, M. Kocher2, M. Herman1, P. Kanovsky1
1 Stroke Centre, Department of Neurology, 2 Department of Radiology, University Hospital, Department of Statistics and Biometry, Palacky University Medical School, Olomouc, Czech Republic

Background and purpose: Mismatch between stroke severity, assessed according to the National Institute of Health Stroke Scale (NIHSS), and the infarct lesion volume on DWI (clinical-diffusion mismatch; CDM) may identify patients with tissue at risk of infarction and has been considered to be a surrogate for PWI-DWI mismatch. The aim was to compare acute ischemic stroke (IS) patients with and without CDM treated by intravenous thrombolysis (IVT) in the infarct growth, clinical outcome and incidence of intracerebral haemorrhage (ICH).

Methods: We retrospectively analyzed 79 IS patients, CDM was defined as NIHSS ≥8 and DWI volume ≤25 ml, non-mismatch as NIHSS ≥8 and DWI >25 ml. DWI infarct volume was measured on admission and 24 hours later. Neurological deficit was evaluated using NIHSS on admission, 24 hours later, and the 90-day clinical outcome using modified Rankin Scale (mRS). Independent Samples, Chi-Square and Fisher Exact tests were used for statistical evaluation.

Results: 37 patients presented CDM, 16 non-CDMs. Patients with non-CDM had significantly higher infarct growth (p=0.039) after 24 hours. CDM patients had significantly higher neurological regression after 24 hours (p<0.01) and significantly better 90 day clinical outcome (mRS 1.2, p=0.002) than non-CDM (mRS 3.6). Incidence of ICH was significantly higher in non-CDM patients (32%, p=0.036), than in CDM (8.1%).

Conclusions: CDM could help identify patients with higher benefit from IVT; patients with CDM had a significantly better clinical outcome and significantly less ICH after 90 days.


P2016

SENSITIVITY AND SPECIFICITY OF COLOR DOPPLER ULTRASOUND IN RELATION TO CAROTID ARTERY ANGIOGRAPHY FINDINGS IN PATIENTS WITH CAROTID ARTERY STENOSIS TREATED AT KBC RIJEKA

I. Sretenja-Linic1, L. Tuskan-Mohar1, I. Antonic1, S. Dunatov1, A. Jurjevic1, B. Budiselic1, D. Curuvija1
1 Clinic of Neurology, 2 Department of Radiology, 3 Department of Thoracic and Vascular Surgery, Surgery Clinic, Clinical Hospital of Rijeka, Croatia

Study Objectives: The aim of this prospective study was to ascertain specificity and sensitivity of the neurosonology Laboratory for Neurology department of Rijeka in detection of carotid artery stenosis in comparison to magnetic angiography (MRA), multi slice computerized carotidography (MSC) and digital subtraction carotidography (DSA).

Examiners: Data for 108 patients (75 male, 33 female), treated at the Neurology clinic from 1.1.2005–31.8.2006, and had CDFI diagnostic was evaluated. The average age of the patients was 67 years (ranging from 44 to 81). North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria were used to determine the degree of stenosis.

Results: 61 MSCT carotidography, 53 DSA and 15 MRA were made. The diagnosis of significant internal carotid stenosis was established: with DSA only in 31%, with MSCT only in 37% and with MRA only in 13% of all patients. For 19% of patients diagnosis was established with 2, or in one case with all 3 methods. The combination of ultrasound findings and these 3 methods has shown 94% (95% CI 89%–97%) sensitivity and 76% (95% CI: 64%–85%) specificity. Positive predictive value (PPV) in our findings was 91% (95% CI: 88%–93%), with negative predictive value (NPV) at 83% (95% CI: 74%–89%).

Conclusion: If the aim of early diagnosis and treatment of carotid artery disease as well as low cost diagnosis and treatment is to be reached, the diagnosis should be established using CDFI diagnostic with only one invasive angiography method in a Neurology Ultrasound Laboratory which fulfils the given criteria of high specificity and sensitivity.

P2017

THE IDENTIFICATION OF THE UNSTABLE CAROTID PLAQUE ON CERVICAL ULTRASOUND AND TRANSCRANIAL DOPPLER

Department of Neurology A. Aristotelian University of Thessaloniki, Ahepa Hospital, Thessaloniki, Greece

Aim: To establish, in patients with carotid plaques, the relationship between cerebrovascular symptoms (amaurosis fugax-AF, cerebrovascular event-CVE, asymptomatic status-A) and plaque echoicity evaluated on ultrasound, stenosis evaluated on ultrasound and embolic count (EC-30 minutes) in the middle cerebral artery (MCA) on transcranial Doppler (TCD).

Methods: 107 patients, with 107 carotid plaques, 16 associated with AF, 34 with CVE and 57 asymptomatic, having stenosis from 50–99% were studied. One plaque per patient was selected; the other side was less than 50% stenosis. The ultrasonic images of carotid plaques were normalised in a computer using two echoic reference points: the GSM (grey scale median) of the blood and the GSM of the adventitia. Normalisation transforms all images so that the GSM of the blood becomes 0–5 and the GSM of the adventitia becomes 180–200. The GSM of the normalised image of the plaques was used as a measure of plaque echoicity. Carotid stenosis and EC were evaluated.

Results: GSM, stenosis and EC separated the 3 groups of carotid plaques (median values for GSM: AF-1, CVE-7, A-36, for stenosis: AF-90%, CVE-77.5%, A-70%, and for EC AF-2.5, CVE-2.5, A-0) (Kruskal-Wallis test, p<0.05). In multinomial logistic regression analysis, only GSM and stenosis and not EC separated the three groups (p<0.05)

Conclusion: These results establish the relationship between the type of cerebrovascular symptom and carotid plaque GSM, stenosis and EC, indicating that these indices can be used to identify the unstable carotid plaques.

P2018

NEUROPATHIC PAIN AFTER STROKE

L.R. Akhmadeeva, G.Sh Rayanova, A.G. Nigmatullin, T.M. Abdrashto
Bashkir State Medical University, Ufa, Russia
Background: Our previous studies showed that pain in many patients makes health related quality of life poorer after stroke.

Objective: To perform a pilot screening for prevalence of neuropathic pain among patients complaining of different pains during the first 6 months after stroke.

Methods: Our group examined 42 patients (26 males and 16 women), mean age 59.8 years (SD=7.1). Most of them (81%) had a stroke for the first time, 69% of patients had ischemic strokes. PainDETECT was used as a screening test for neuropathic pain.

Results: Most probable neuropathic pain (scores 19–38) was found in 6 patients (14.4%); most probable nociceptive pain (scores <12) in 16 patients (38%). Every second patient (47.6%) had scores between 13 and 18. The mean score for pain was M=11.45 (SD=5.7; m=0.87). The majority of patients (34 out of 42) experienced pain in the weak extremity. In 6 patients (mostly younger men) pain was severe (VAS between 80 and 100 out of 100).

Conclusion: Neuropathic component is often seen in patients with pain after strokes. It is important to differentiate it from other pains and to prescribe specific medicines and management. We thank Prof. A. Danilov (Moscow) for the idea and questionnaire and the Russian President’s Grants Board for supporting this study.

P2019
EXTRA-CRANIAL CAROTID STENOSIS (ECS) IS NOT RARE ALL OVER THE ORIENT
K. Basiri¹,², F. Ashvari¹
¹Department of Neurology, Alzahra University Hospital, ²Department of Neurology, Kashani University Hospital, Isfahan, Iran

Introduction: Asians have been reported to have extremely low prevalence rate of extra-cranial carotid and vertebral artery disease. Data about extra-cranial artery disease in Iranian stroke patients is unavailable. In the current study, prevalence of carotid and vertebral artery stenosis in the Iranian population was determined and compared with the frequency of extra-cranial artery disease in other Asian populations.

Methods: Documented cases of ischemic stroke were evaluated by Duplex Ultrasonography (DU) for any evidence of carotid plaque, flow disturbances and increase in peak systolic Velocity (PSV). Then the ratio of ICA/CCA peak systolic velocities were measured and the degree of stenosis was calculated according to the observed spectral waves.

Results: 150 stroke patients were evaluated. Unilateral carotid stenosis or occlusion was detected in 38 patients (25.3%) and bilateral stenosis in another 10 patients (6.6%). In 39 patients (26%) stenosis was in the ICA and in 9 patients (6%) it was located in CCA. 18 patients (12%) were found with greater than 50% carotid stenosis.

Conclusion: Extra-cranial Carotid stenosis (ECS) was not infrequent and was located for the most part in ICA. We conclude that ECS is not uncommon in the Iranian population as it is in some other Asian populations.

P2020
ELEVATED INFLAMMATORY MARKER IL-6 IN LACUNAR STROKES
M. Beridze¹, M. Janelidze¹, R. Shakharishvili², J. Ramsden³
¹Department of Neuromedicine, State Medical University, Tbilisi, Georgia, ²Institute of Advanced Study, Collegium Basilea, Basel, Switzerland

Background and aims: Several patients retain the high levels of blood proinflammatory indices even in subacute stages of stroke. Study purposed to detect whether it is associated with disease etiology and designed to compare the blood proinflammatory cytokines in different etiological subgroups on 15th day after stroke onset.

Methods: 85 acute stroke patients aged 45 to 70 have been investigated. Patients were grouped according to TOAST etiological criteria as Atherosclerosis, Cardioembolism, Lacunar Strokes. All non modified and modified risk factors of stroke were registered. Blood cytokine levels defined by ELISA method. Control consisted with 25 healthy persons. The data obtained were analyzed by computer software SPSS-10.0. Means were calculated by Student’s t-test. Pearson correlation and Multivariate logistic regression were used.

Results: The blood levels of IL-1β and TNF-α did not differ significantly between etiological groups, but found to be increased against control (p<0.05). The level of IL-6 was elevated in lacunar strokes compared to other etiological subgroups and control (18.2±3.7 versus 13.4±2.7 versus 12.7±2.1 versus 12.3±3.8; p<0.05). Multivariate logistic regression analysis found the positive correlation between arterial hypertension and mean predicted probability of blood IL-6 levels on 15th day of disease. Correlation Coefficient r=+0.12; p<0.05.

Conclusion: Probably, along with modification of hypertension the anti-inflammatory approach will be beneficial for secondary prevention of lacunar strokes.

P2021
MOUNTAINS ARE NOT AN OBSTACLE TO THROMBOLYSIS: EXTENSION OF CLINICAL TRIAL RESULTS TO THE TRENTINO REGION
D.M. Bonifati¹, C. Boninsegna², E. Gremes³, R Tanel¹, M. Buganza¹, E. Tranquillini¹, A. Morini¹, S. Maranongi¹, P. Girardi¹, S. Filippioni¹, A. Zini¹, P. Iseppi¹, D. Orrico¹
¹Unit of Neurology, Department of Internal Medicine, Santa Chiara Hospital, ²Department of Emergency, Azienda Provinciale Servizi Sanitari, Trento, Italy

Objectives and background: Not always patients enrolled in clinical trials correspond to patients in common clinical practice. To evaluate retrospectively patients treated with thrombolysis in our Stroke Unit in Trentino, a mountainous region in North Italy.

Materials and methods: We evaluated patients treated with thrombolysis since May 2005. SITS-MOST protocol was applied to all patients. We considered the way and timing of arrival and NIHSS scale was used to measure clinical outcome.

Results: 18 patients with a mean age of 65.7 met the SITS-MOST criteria. 5 patients arrived from other district hospitals in mountainous valleys. 11 patients arrived by ambulance and 7 by helicopter. Mean time of arrival was 72 minutes (range 27–121), brain CT scan was performed after a mean of 103 minutes (range 50–172) and treatment began after a mean 149 minutes (range 120–180). 7 patients markedly improved (NIHSS ³ 3 at the discharge), 5 patients improved with a NIHSS scale between 5 and 8 while four were stationary. 2 died: one for aortic dissection and one for hemorrhagic stroke. Intracranial hemorrhage, needed surgical intervention, developed in one patient. Between side effects we had one mild orolingual angioedema.

Conclusion and discussion: Although the mountainous nature of our region, around 1% of all strokes (and 4% of all the patients admitted) were treated with thrombolysis. Clinical results are very similar to those derived from clinical trials. This suggests the applicability of this acute treatment in different regions and clinical practice settings, providing a large network has been set up.
MIGRAINE-INDUCED STROKES OF ATYPICAL LOCATION

A. Boutsi, C. Balla, N. Taskos, I. Milonas
Department of Neurology B, Ahepa University Hospital, Aristotle University, Thessaloniki, Greece

Introduction: Migraine is claimed to be a rare risk factor for ischaemic strokes. True migraine-induced strokes are mainly occipital or cerebellar and associated with the posterior cerebral circulation. Supratentorial white matter lesions are also associated frequently with migraine. Nevertheless, true migraine-induced strokes can be observed in non typical brain regions. Two of them are described below.

Patients and methods: Case 1. A 24-year-old woman presented with right hemiparesis, dysarthria and right facial palsy; established 6 hours after the onset of a migraine attack and deteriorated during the next few hours to right hemiplegia. Case 2. A 32-year-old woman presented with right hemiparesis, right upper quarter hemianopsia, right proprioceptive hypoesthesia established 2 hours after a migraine attack. In both cases, the women suffered from migraine without aura established following International Headache Society’s criteria and had no classical risk factors for stroke.

Results: Magnetic Resonance Imaging: Case 1: infarct in the posterior peduncle of the left internal capsule with subcortical white matter hyperintensities in T2-weighted images. Case 2: infarct of left hippocampus, thalamus and inner part of the occipital lobe. In both cases, Magnetic Resonance Angiography, extracranial ultrasonography, transcranial Doppler, transthoracic and transoesophageal echocardiography and all tests for blood functions (including autoimmune and coagulation markers) were normal.

Conclusion: Even if the majority of migraine-induced strokes is located in the territory of the cerebral posterior circulation, the atypical location of a stroke cannot exclude the possibility that this arises from a migraine attack when all paraclinical investigations are negative.

OBSTRUCTIVE SLEEP APNOEA SYNDROME AND HEART FAILURE IN PROGRESSIVE STROKE PATIENTS

I.T. Burduladze, T.G. Bostiashvili, R.R. Shakarishvili
Department of Neurology, Sarajishvili Institute of Clinical Neurology and Neurosurgery, Tbilisi, Georgia

Background: Previous investigations prove a high incidence of stroke among persons with obstructive sleep apnoea syndrome (OSAS). At the same time, high frequency of OSAS have been mentioned in patients with heart failure (HF). Purpose of present study was to investigate the possible haemorrhological effects of OSAS on the cardiovascular system in progressive stroke (PS) patients.

Subjects and methods: 25 male patients (mean age 61.0 years) with PS were investigated. The following haematological parameters were evaluated: erythrocyte aggregability index (EAI), prothrombin index (PI), hematocrit (Hct). In all cases sleep EEG and echocardiomonitoring were performed.

Results: We found that in patients with PS accompanied by HF (n=10) trustworthy changes of haematological data were in evidence in cases of OSA than in patients without HF (n=15). It was especially increased EAI by 16% (p=0.001), Hct by 10% (p=0.001) and PI by 6% (p=0.1). Increased EAI was correlated with low haemoglobin saturation and increased left ventricular transmural pressure.

Conclusions: Haemorrhological effects of OSAS on HF may play an important role in development of ischemic stroke besides well known mechanical, haemodynamic and neurohumoral effects.

PLATELET P-SELECTIN EXPRESSION PREDICTS THE SEVERITY OF ACUTE ISCHEMIC STROKE

J.-K. Cha1, Y. M. Jo2, J.H. Bae3
1Department of Neurology, 2Department of Neurology, 3Dong-Eui Hospital, Busan, South Korea

Background: Platelet activation is an important pathophysiology in acute ischemic stroke. However, there has been little information about the relationship between the extent of platelet activation and clinical severity in ischemic stroke. We investigated the hypothesis that the extent of platelet activation might be a useful marker to reveal the clinical severity of acute ischemic stroke.

Methods: We measured the platelet aggregability for adenosine diphosphate (ADP) or collagen and surface expression of P-selectin in ischemic stroke patients in acute phase (<24 hrs). National Institutes of Health Stroke Scale (NIHSS) score was evaluated at admission day. Also, we scored the Barthel index (BI) after 90 days of ischemic events.

Results: The platelet aggregability for ADP or collagen and the extent of P-selectin expression were significantly higher in acute ischemic stroke than in normal subjects. The extent of platelet P-selectin expression significantly correlated with NIHSS (r=0.359, p=0.004) at admission day and the Barthel index (r=0.412, p<0.001) at 90 days after ischemic events.

THE MOST COMMON RISK FACTORS AND SEX DIFFERENCES IN YOUNG ADULTS WITH ISCHEMIC STROKE

L. Dezmalj Grbelja, J. Bosnjak, R. Covic Negovetic, V. Seric, V. Demarin
University Department of Neurology, University Hospital Sestre Milosrdnice, Zagreb, Croatia

Background: Stroke takes the leading position in morbidity and mortality in Croatia and presents a considerable public-health problem. We evaluated sex differences in the most common risk factors in young adults.

Methods: We retrospectively analyzed the data of patients between the age of 19 and 45, who were admitted to the University Department of Neurology, University Hospital “Sestre milosrdnice”, in the period between 1.1.2002. and 31.12.2006.

Results: 3193 patients with acute stroke were admitted, 93 (2.88%) were younger than 45. Ischemic stroke was diagnosed in 51 patients (55.43%), 30 male (58.82%) and 21 female (41.18%). The most common risk factors in men were hypertension (13; 43.33%), smoking (14; 46.66%), hyperlipidemia (11; 36.66%), alcohol abuse (7; 23.33%), heart diseases including cardiomyopathy, arrhythmia and valvular abnormalities (6; 20%), haemato logic abnormalities (2; 6.66%) and diabetes (1; 3.33%). In women the most frequent risk factors were hyperlipidemia (9; 42.85%), hypertension (6; 28.57%), heart diseases and oral contraceptives (4; 19.04%), smoking (3; 14.28%), illegal drugs (2; 9.52%) and alcohol abuse (1; 4.76%).

Conclusion: Risk factors for ischemic stroke in young adults have similar distribution as in older patients, except diabetes and heart disease, in both men and women. Hypertension, alcohol and smoking are more frequent in men, while hyperlipidemia and heart diseases are equally present. Considerable cause in women are oral contraceptives. In a great number of patients we did not find any of
the most common risk factors, so we have to look for less frequent causes as immunologic and haematologic disorders, and include such tests in the diagnostic algorithm.

P2026
VERTEBRAL ARTERY HYPOPLASIA IN PERSONS WITH BLOOD CIRCULATION INSUFFICIENCY IN THE VERTEBO-BASILAR ARTERY SYSTEM
D.S. Druzhinin, N.V. Pizova
Department of Neurology, Yaroslavl State Medical Academy, Yaroslavl, Russia

The Aim: To detect the frequency of vertebral artery hypoplasia occurrence at persons with blood circulation insufficiency in the vertebo-basilar artery (VBA) system. 1549 patients with chronic brain blood circulation insufficiency in VBA system (634 men – 40.9% and 885 women – 59.1%) passed through the examination using the ultrasonic research of vessels in duplex and triplex scanning modes.

Results: 369 persons (23.8%) were found to have the vertebral arteries (VA) pathology. 14.9% (n=55) among these patients had VA hypoplasia: 37 women (67%) and 18 men (33%). 5 men (9.0%) and 2 women (3.6%) under the age of 30 years, 6 men (10.9%) and 25 women (45.4%) from 30 till 50 years and 7 men (12.7%) and 9 women (16.3%) over 50 years had VA hypoplasia. The right VA hypoplasia proved to be more frequent (n=39–70%) than the left VA hypoplasia (n=16–30%). In 12 observations (21%) the basilar artery blood flow was 10–30% below the normal value. In the remaining 43 cases (79%) the blood flow was reduced when performing the rotation test. Moreover, 16 observations (29%) discovered the combination of VA hypoplasia with pathological deformation of both internal carotids, mainly S and/or Z-type.

Conclusions: The VA hypoplasia was observed in 14.9% of cases in persons with chronic brain blood circulation insufficiency in VBA system. In 1/3 of the cases there was a combination of VA hypoplasia with pathological deformation of both internal carotids.

P2027
CORRELATION BETWEEN CARDIO-EMBOLIC STROKE AND VENTRICULAR THROMBOSIS AFTER ACUTE MYOCARDIAL INFARCTION
C.A. Panae, G. Vulpe, H. Nicloae, D.G. Stefanescu, I. Codita, S. Petrescu, M. Grasu
Neurology Department, Elias Emergency University Hospital, Bucharest, Romania

Background: The cardio-embolic stroke represents 20% of ischemic stroke. The untreated acute myocardial infarction complicates frequently the formation of ventricular aneurysm. The thrombosis of the left ventricle appears in the first 5–10 days, especially in the anterior myocardial infarction. Goal. This study wanted to appreciate the predictive factors for cardio-embolic strokes to patients with acute myocardial infarction.

Method: Observational prospective study of patients with ventricular thrombosis after acute myocardial infarction and cerebral embolism. The predictive factors for intraventricular thrombosis were analysed together with the risk factors for cerebral cardioembolism. This is an ongoing study.

Results: 3.8% (7) of 183 hospitalised patients with acute myocardial infarction have thrombosis in the apical aneurysm. The cerebral complication may be either micro or macroembolisation. 5.1% (6) of the 117 patients with cardio-embolic stroke has a thrombosis in the left ventricle. The predictive factors for cerebral embolisation are: ejection fraction lower than 65%, anterior infarction, thrombosis in the left ventricle and diskinesis of the left ventricle. It appears more often in the first 72 hours.

Conclusion: The prevalence of cardio-embolic stroke is low, but it has a fatal risk or leads to high invalidity, because of severe affection of both central and coronary vessels. The diagnosis is difficult. In Romanians the number of ventricular thrombosis is higher because of late diagnosis of myocardial infarction due to either less specific manifestation or misdiagnosis by lack of specific investigations. Patients with acute myocardial infarction should be neurologically evaluated to prevent a cerebral embolism.

P2028
HYPOGLOSSAL PARESIS – TWO CASES
B.A. Jacobsen, N.J. Brautaset
Neurological Department, Vestfold Hospital, Tonsberg, Norway

We will present two patients admitted to our Neurological department because of half sided facial pain and hypoglossal paresis.

Patient 1: 52-year-old male with Crohn’s disease, otherwise healthy. He woke up with intense pain in the left temporal part of the head and the left jaw. After six days he developed ipsilateral peripheral hypoglossal paresis without other neurological symptoms. The pain subsided after a couple of weeks. At control examination after 6 months he had no signs of hypoglossal paresis.

Patient 2: 48-year-old male with unremarkable past medical history. He developed sub acute right facial pain and blurred speech. 6 days later he was admitted to hospital with right hypoglossal paresis and slight Horner’s syndrome. The facial pain disappeared after a few days. At control examinations 5 weeks after the symptoms started, he felt healthy and neurological findings were unremarkable. Diagnostic workup and differential diagnosis are presented. In both cases, MRI angio showed that the symptoms were caused by dissection of the internal carotid artery. This diagnosis should be considered in isolated paresis of the caudal cranial nerves, especially when there are simultaneously ipsilateral facial pain and Horner’s syndrome.

P2029
PROGNOSTIC FACTORS OF POOR OUTCOME OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE
D. Kuljic-Obradovic1, A. Bezymarevic1, S. Medic1, B. Mrusulja2
1“Sveti Sava” Hospital, Belgrade, ‘Clinical Hospital Centre “Dr Dragisa Misovic”, Belgrade, Serbia

Background and aims: The aim of the study was to identify prognostic factors and construct a rational set of criteria for prediction of short-term outcome of spontaneous intracerebral haemorrhage (ICH).

Methods: We studied 117 patients with ICH using a standard protocol: medical history, physical and neurological examination, Glasgow Coma Scale, CT scan and outcome upon discharge (good outcome: improvement of neurological status; poor outcome: neurological impairment or death). ICH was graded according to size (small <30 ml, medium 30–60 ml, large >60 ml), localization (putaminal, thalamic, pontine, cerebellar, lobar haemorrhage) and intraventricular extension.

Results: There were 40.3% female and 59.7% male patients with ICH, age range 39 to 90. Good outcome was noted in 37.9% of these patients while 62.1% had poor outcome with mortality rate 43.1%. The patients with ventricular extension were more likely to exhibit poor outcome (77.4% vs. 30.6%), as well as the patients with impaired consciousness (p<0.01). Large haemorrhages were more frequently followed by poor outcome (93.3%) than medium
(50%) and small (33.7%). There were no significant differences between patients with poor and favourable outcome regarding to sex, age, localization or risk factors for ICH (hypertension, alcohol abuse, diabetes mellitus, cigarette smoking, hyperlipidemia, previous stroke, heart disease).

**Conclusions:** The most important predictors of poor short-term outcome of ICH were the size of haemorrhage (p<0.01), ventricular extension (p<0.01) and impaired consciousness (p<0.01). Sex, age, localization of ICH and risk factors do not influence significantly the prognosis of ICH.

**P2030**

**SUDDEN ONSET OF FOCAL NEUROLOGICAL SYMPTOMS IN PREGNANCY: MIGRAINE IS MORE COMMON THAN ISCHEMIA**

A. Liberman, D. Karuss, T. Ben-Hur, R. Leker
Neurology Department, Hadassah-Hebrew University Hospital, Jerusalem, Israel

**Background:** Sudden onset of focal neurological symptoms in young healthy pregnant women is not infrequent and leads to extensive evaluations.

**Objective:** To determine the pathogenesis of focal neurological symptoms in previously healthy pregnant women and to set up prognostic variables for target screening in appropriate patients.

**Methods:** Previously healthy pregnant women, presenting to our hospital with acute neurological symptoms, were recruited. Investigation included MRI/ MRV protocol, cardiovascular tests (echocardiography, duplex ultrasonography) and hypercoagulability tests. The outpatient follow-up was estimated at 12 months.

**Results:** 9 patients were enrolled, mean age of 32.6 (range 24–41). The mean pregnancy age at the symptoms’ onset was 35 weeks (range 17–44). Presenting symptoms included dysphasia (5), hemisensory (4) or hemimotor (4) syndrome. In 4 patients the symptoms were preceded by scintillating scotomas and in 6 patients were followed by throbbing headache (first-ever in the lifetime). Only one patient had evidence of frank infarction on MRI. Echocardiography was normal in all except one patient, which showed a mobile cardiac mass interpreted as a thrombus, with normal MRI and no evidence for stroke on follow up. Carotid duplex and hypercoagulability tests were negative in all patients. None of our patients had true ischemic event during follow-up.

**Conclusions:** The occurrence of focal neurological symptoms in pregnancy is frequently preceded by aural visual phenomena and may be attributed to a first-ever migraine attack. Frank ischemia appears to be less common than migraine, therefore a brain MRI and extensive evaluations may not be warranted in such patients.

**P2031**

**CLINICAL CHARACTERIZATION OF YOUNG PATIENTS AFTER CRYPTOGENIC STROKE/TIA DIAGNOSED FOR PATENT FORAMEN OVALE PREVALENCE**

1Neurology Department, Oswiecim Hospital, Oswiecim, Poland
21st Department of Cardiology, 3Department of Neurology, Ageing, Degenerative and Cerebrovascular Diseases, Silesian University of Medicine, Katowice, Poland

**Background:** Patent foramen ovale (PFO) is considered a cause of cryptogenic stroke and risk factor for the neurological events in group of young patients (pts). The goal of this study was to find clinical characteristics of young pts after cryptogenic stroke/TIA with and without PFO.

**Methods:** We investigated 133 consecutive pts diagnosed in our department due to cryptogenic stroke (91 pts) and TIA (29 pts) or other neurological symptoms in years 2004 and 2006. Stroke risk factors such as hypertension, hypercholesterolemia, diabetes, smoking, atrial fibrillation, oral contraception, migraine and crural varices were assessed. Transthoracic echocardiography, multiplane TEE with contrast (agitated saline) and Valsalva manoeuvre, and biochemical tests were performed. A PFO was identified in 82 cases (61%), (female: 54, age 40±23 yrs) and in the remaining 51 pts PFO was excluded (female: 32, age 44±25 yrs).

**Conclusions:** PFO pts are characterized by less frequent occurrence of atherosclerotic risk factors such as hypertension, hypercholesterolemia, diabetes, and also atrial fibrillation. In PFO group we observed higher number of crural varices, migraine and oral contraception intake.

**Results:**

<table>
<thead>
<tr>
<th></th>
<th>PFO (+)</th>
<th>PFO (-)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>28.0</td>
<td>57.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>6.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>31.7</td>
<td>46.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypercholest.</td>
<td>34.1</td>
<td>56.5</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1.2</td>
<td>8.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Oral contraception</td>
<td>26.8</td>
<td>15.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Crural varices</td>
<td>23.2</td>
<td>4.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Headache (migraine)</td>
<td>85</td>
<td>53.5</td>
<td>0.006</td>
</tr>
</tbody>
</table>

**P2032**

**EFFICACY AND SAFETY OF PERCUTANEOUS CLOSURE OF PATENT FORAMEN OVALE IN SECONDARY PREVENTION OF CRYPTOGENIC STROKE/TIA**

1Neurology Department, Oswiecim Hospital, Oswiecim, Poland
21st Department of Cardiology, Department of Neurology, Ageing, Degenerative and Cerebrovascular Diseases, Silesian University of Medicine, Katowice, Poland

**Background:** In young patients (pts) who underwent cryptogenic stroke patent foramen ovale (PFO) is considered a cause and risk factor for the next neurological events. Percutaneous closure of PFO has been proposed as an alternative to anticogulatation treatment. We investigated efficacy and safety of percutaneous closure of PFO in secondary stroke prevention.

**Methods:** 60 pts (20 males/40 females) at a mean age of 41±19 years underwent catheter closure of their PFO. 36 pts had ischemic stroke, 17 pts had TIA and 8 pts had stroke and TIA. In 30 cases stroke was related to physical exercise (Valsalva manoeuvre). The implantation procedures were performed in local anaesthesia, under transoesophageal echocardiography (TEE) and fluoroscopy. As a standard procedure control TEE 6–9 months post PFO closure was performed.

**Results:** In 28 cases PFO was associated with atrial septum aneurysm (ASA), in 4 cases with Chiari network. The implantation procedure was successful in all pts. In 58 cases Cardia/Intrasent occcluder was used and in remaining 2 cases Amplatz and StarFlex. In 1 case atrial fibrillation was observed in perioperdural period which converted to sinus rhythm spontaneously. Two patients developed a haematoma, and then in 1 case varicose vein inflammation at the catheter site requiring pharmacological treatment. At a mean
follow-up of 13±13 months, there were no deaths. One patient suffered from minor stroke. Control TEE documented complete closure in 42 cases of 45 pts who completed a 6–9 month follow-up. In 3 cases we observed minor peri-device residual shunt in TEE.

Conclusions: Percutaneous PFO closure seems to be effective and safe technique in prevention of recurrent stroke. However, in some cases post procedural residual shunt may occur.

P2033

PFO AND ATRIAL SEPTUM ANATOMICAL CHARACTERISTICS IN PATIENTS DIAGNOSED DUE TO A CRYPTOGENIC NEUROLOGICAL EVENT

J. Machowski1, E. Konarska-Kuszewska1, P Weglarz2, K. Spisak-Borowska1, A. Drzewiecka-Gerber1, J. Krauze1, A. Filipecki1, K. Wita2, J. Drzewiecki2, M. Trusz-Gluza2, G. Opala3

1 Neurology Department, Oswiecim Hospital, Oswiecim, 21st Department of Cardiology, 3Department of Neurology, Ageing, Degenerative and Cerebrovascular Diseases, Silesian University of Medicine, Katowice, Poland

Background: Patent foramen ovale (PFO) and associated structures like atrial septum aneurysm (ASA) are considered a cause of cryptogenic stroke and risk factor for the neurological events in a group of young patients (pts). The goal of this study was to find characteristics of these structures in pts after cryptogenic stroke/TIA with and without PFO.

Methods: We investigated 133 consecutive pts, diagnosed in our department due to cryptogenic stroke (91 pts) and TIA (29 pts) and other neurological symptoms in the years 2004 and 2006. Thoracic echocardiography, multiplane TEE with contrast (agitated saline) and Valsalva manoeuvre were performed. PFO was identified in 82 cases (61%), (female: 54, age 40±23 yrs) and in the remaining 51 pts PFO was excluded (female: 32, age 44±25 yrs). We concentrated on PFO channel and ASA assessment in this group. ASA was classified as small (≤10mm amplitude) and (large >10mm) and also PFO channel was classified as small (1–3 mm) and (large >4 mm). TEE examinations were assessed for Chiari network prevalence.

Conclusions: We observed about 60% PFO prevalence in patients diagnosed due to cryptogenic ischemic neurological event. PFO was associated with higher ASA prevalence, especially large ASA which was more frequent in a group with large PFO. Chiari network was seldom and was observed only in PFO group.

Table 1. ASA prevalence in PFO group

<table>
<thead>
<tr>
<th>ASA (%)</th>
<th>Group with PFO</th>
<th>Group without PFO</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small ASA (%)</td>
<td>37</td>
<td>3.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Large ASA (%)</td>
<td>40.2</td>
<td>5.9</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 2. PFO and ASA characteristics

<table>
<thead>
<tr>
<th>Prevalence (%)</th>
<th>Small PFO channel</th>
<th>Large PFO channel</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFO (%)</td>
<td>62.5</td>
<td>37.5</td>
<td>0.01</td>
</tr>
<tr>
<td>PFO with ASA (%)</td>
<td>40.7</td>
<td>71.4</td>
<td>0.03</td>
</tr>
<tr>
<td>PFO with small ASA (%)</td>
<td>8.6</td>
<td>4.3</td>
<td>ns</td>
</tr>
<tr>
<td>PFO with large ASA (%)</td>
<td>37.1</td>
<td>96.6</td>
<td>0.03</td>
</tr>
</tbody>
</table>

P2034

THE ROLE OF IMMUNE DISORDERS IN CLINICAL DYNAMICS OF STROKE

M. Megrelishvili, M. Beridze, M. Janelidze, R. Shakarishvili

Department of Neurology, Tbilisi State Medical University, Tbilisi, Georgia

Objective: To investigate the role of immune reactions in clinical dynamics of acute ischemic stroke.

Methods: 40 patients with same initial severity of acute ischemic stroke (NIHSS=14.15) were investigated. Neurological status assessed on admission on 7th day from symptoms onset for evaluation of clinical dynamics of disease. Blood mixed culture of autologous lymphocytes (MCFL) was researched and number of blood blasttransformed lymphocytes calculated under the light microscope. Control consisted with 15 healthy volunteers. Means were defined by Student’s t-test. ANOVA analysis and Pearson correlation were used.

Results: All stroke patients revealed the increased number of blood blasttransformed lymphocytes compared to control (p<0.05), while the 17 stroke patients found to have significantly elevated number of blasttransformed lymphocytes of MCAL against other stroke patients and control (p<0.05). On 7th day 14 patients showed the increased NIHSS score against initial date, with mean increase (2.5±0.4), 7 patients did not change the initial NIHSS significantly and 19 patients showed the decreased NIHSS with mean decrease (4.8±1.1). Correlation analysis found the significant positive correlation between the increasing number of blood blasttransformed lymphocytes in MCAL and NIHSS score on 7th day of stroke onset. r=0.38; p<0.01;

Conclusion: Non-recognition of their own antigens by blood lymphocytes indicates the development of autoagressive reactions in acute stage of stroke and is associated with negative dynamics of disease.

P2035

MENINGOVASCULAR SYPHILIS: AN UNFREQUENT CAUSE OF STROKE

J.M. Campillo, A.H. Valverde, R.C. Ginesal

Department of Neurology, Hospital Amadora-Sintra, Amadora, Lisboa, Portugal

Background: Meningovascular syphilis comprises 15% of cases of symptomatic neurosyphilis. It develops 5–10 years after infection. Its manifestations include headache, dementia, psychosis and stroke due to progressive arteritis. Diagnosis is based on analysis of cerebrospinal fluid (CSF).

Methods: Patient 1: A 23-year-old man was admitted to hospital due to left hemiparesis. A brain CT and a magnetic resonance showed bilateral parietal, left lenticular and right pontine infarctions. A magnetic resonance angiography showed basilar artery stenosis. Treponemic serology was positive (TPHA 1/20480). CSF analysis showed lymphocytic pleocitosis (45 cells/mm³) with increased proteins (154 mg/dl). Treponemic serology in CSF was also positive (1/20480).

Patient 2: A 37-year-old man was admitted to hospital due to left hemiparesis. A brain CT and a magnetic resonance showed right pontine and left temporal acute infarctions. An angiography showed severe stenosis in left middle cerebral, left posterior, left PICA and basilar arteries. Treponemic serology was positive (1/20480). CSF analysis showed 35 lymphocytes/mm³, without protein increase. Treponemic serology in CSF was also positive (1/20480).

Results: The onset was apoplectic in both patients. Imaging showed ischemic lesions in different arterial territories. Angiography techniques lead to the diagnosis of intracranial stenosis. Lumbar puncture showed lymphocytic pleocitosis and positive treponemic serology in both cases.

Conclusions: Meningovascular syphilis should always be considered as a possible etiology of stroke. Different arterial territories may be involved. Intracranial stenoses are usually found, due to progressive arteritis. The analysis of CSF plays crucial role in the diagnosis.
P2036
ATHEROSCLEROSIS IS A RISK FACTOR FOR LEUKOARAIOSIS IN PATIENTS WITH ISCHEMIC STROKE
M.D. Minajlovic1, E. Ben-Assayag2, I. Bovai3, L. Shopin2, S. Shenhar2, S. Berliner1, T. Nissel1, I. Shapira1, N.M. Bornstein1
1Institute of Neurology, Clinical Centre of Serbia, Belgrade, Serbia
2Department of Neurology, 3Department of Internal Medicine D, Tel-Aviv Sourasky Medical Centre, Tel-Aviv, Israel

Objectives: Previous studies have shown that white matter lesions are associated with increasing age, hypertension, diabetes and history of stroke. Although several lines of evidence suggest a role of atherosclerotic processes in atherothrombotic vascular events, their involvement in leukoaraiosis remains to be determined. Our study examines the association between atherosclerosis, reflected as IMT and carotid plaques, lipid profile and leukoaraiosis in a group of ischemic stroke patients.

Methods: 164 consecutive ischemic stroke patients were included (mean age 66.7±3.4 years). All patients underwent brain computed tomography, carotid duplex with measurements of IMT, and lipid profile.

Results: 44% of patients were found to have 1 or more white matter lesions on CT images located in frontal, parietal or occipital region. 62.5% patients had leukoaraiosis located in at least 2 brain regions, and 13.8% had leukoaraiosis in all regions. Mean IMT was significantly higher in stroke patients with leukoaraiosis (p=0.004) compared to those without it. Also, leukoaraiosis was associated with carotid plaque occurrence (χ²=6.154, p=0.013). HDL-cholesterol was found to be significantly lower in the leukoaraiosis patients (p=0.041). In logistic regression analysis, including age, gender, body mass index, and all vascular risk factors, leukoaraiosis was found to be associated with age and IMT (O.R. 1.04, 95% CI 1.01-1.071, p=0.009; O.R. 13.058, 95% CI 1.509-113.014, p=0.02; respectively).

Conclusions: In our acute ischemic stroke patient cohort, the incidence of leukoaraiosis is high. Advanced atherosclerotic process (expressed by significantly increased IMT) is associated with more widespread atherosclerotic lesions, comprising large, as well as small cerebral arteries.

P2037
LATERALITY OF HEMISPHERIC STROKES: FUNCTIONAL OUTCOMES OF PATIENTS MANAGED IN A STROKE REHABILITATION UNIT
M. Muzzam1, H.G. Shetty1, I. Singh1, T. Nicholson1
1Regional Stroke Unit, Cardiff Royal Infirmary; 2Department of Geriatric Medicine, University Hospital of Wales, Cardiff, UK

Background and aim: Studies have shown associations between hemispheric laterality and stroke outcomes including functional, cognitive and behavioural. We aim to assess the impact of hemispheric laterality on functional outcomes.

Methods: A retrospective analysis of 325 stroke patients identified from Stroke Rehabilitation Unit (SRU) database between 1st June, 2003 and 1st June, 2006. Amongst these, 105 patients had hemispheric strokes (guided from imaging). Other data recorded include demography, admission and discharge activities of daily living using modified Rankin and place of discharge. Data was analysed using SPSS (p<0.05 significance level).

Results: The majority (88.6%) had unilateral-hemispheric lesions (right, RH=40%; left, LH=48.6%) and the remaining bilateral. Mean age was 72.6±11.1 years with slight female preponderance (54.3%). On admission, 7.4% patients were independent for RH (LH=11.7%) and 54.7% severely disabled (LH=37.3%). At discharge, 21.4% patients were independent for RH (LH=23.6%) and 26.1% severely disabled (LH=29.4%). No significant differences in the Rankin scores found on admission (p=0.092) or at discharge (p=0.898). However, significant differences (p=0.047) shown for discharge destination: own home constituted 72.5% (RH=39.6%; LH=60.3%) whilst care homes, 37.3% (RH=63.3%; LH=36.4%).

Conclusion: We found no difference in the functional outcome in relation to hemispheric laterality. However, patients with LH lesions appear more likely to be discharged home in comparison to RH. We propose further investigation by a prospective study to explore this difference.

P2038
PREDICTING VALUE OF SILENT LACUNAR BRAIN INFARCTS IN PATIENTS WITH HYPERTENSION
M. Prokopovich1, Y. Varakin1
1Institute of Neurology, Moscow, Russia

The purpose: The aim of our study was to investigate the relationship between silent lacunar brain infarctions and the incidence of cerebrovascular diseases (CVD) including stroke, TIA that occurred in patients with essential arterial hypertension in the frames of a 10-years prospective study.

Methods: A 10-years follow-up study including 98 patients with essential arterial hypertension. All of them were thoroughly examined in the Institute of neurology and in the Institute of clinical cardiology in 1990–1992 (men aged 45–55 years). The brain was evaluated by means of CT-scan. At initial examination: no abnormalities in the brain were in 89% (88/98), the silent lacunar infarcts were detected in 11% (10/98) of patients. Infarcts foci were located in deep white-matter (20%), basal ganglia (70%) and brainstem (10%). It was estimates. The incidence of new cases CVD was estimated.

Results: The incidence of CVD was statistically significant in patients with silent lacunar brain infarctions. New cases of CVD were noted in 60% (6/10) of patients with silent lacunar brain infarctions and in 9% (8/88) (p=0.0004) of patients without any abnormalities in the brain (RR=6,6 [2.3; 13.5]). We studied the relationship between silent lacunar brain infarctions and time of onset of CVD (the Gehans Wilcoxon test was used) (p=0.05).

Conclusions: The silent lacunar brain infarctions are a prediction factor of CVD development in patients with essential arterial hypertension.

P2039
THE IMPORTANCE OF CAROTID STENOSIS EVALUATION IN STROKE PREVENTION IN HYPERTENSIVE DIABETIC AND NON DIABETIC PATIENTS
C.R. Revnic1, C. Popa2, F. Revnic1
1Faculty of General Medicine, University of Medicine and Pharmacy “Carol Davila”, 2Department of Neurology, Cerebrovascular Disease Institute “Vlad Voiculescu”, 3Biology of Aging Department, National Institute of Gerontology and Geriatrics “Ana Aslan”, Bucharest, Romania

Background: The evaluation of intima thickening (IMT) of carotid artery is an important parameter in preclinical diagnosis of atherosclerosis and stroke risk in hypertensive elderly patients. The aim of study was to see if there is a relationship between thickening of the carotid artery wall and brain damage in hypertensive elderly patients with/without diabetes.

Material and methods: Our study has been done on 150 patients admitted to the Neurological Clinic over 3 years. At admission, the patients were neurologically examined and divided into two groups
of 75 patients in each: group A with type II diabetes and group B non-diabetes, symptomatc with stroke or asymptomatic, mean age: 64.3±6.8 years old. Carotid Doppler ultrasound examination and cranial NMR were performed.

**Results:** NMR findings were related, to white matter lesions and infarctions; they were more frequent in the hypertensive diabetic group. In hypertensive non-diabetics, there were insignificant correlations between abnormal NMR findings and thickening of carotid wall versus non-diabetic. In diabetes, the associations among cortical lesions, clinically symptomatic stroke, and increase in carotid wall thickness were found to be statistically significant in comparison with non-diabetics. NMR abnormalities were present in 92% patients in group A and 70% patients in group B consisting of arterial constriction or an atheromatous plaque confirmed by Doppler examination.

**Conclusion:** Measurements of carotid wall thickness via Doppler were considered to be valuable in prediction of brain damaged risk and future stroke due to hypertension in diabetic and non-diabetic patients.

### P2040

**ATRIAL MYXOMA CAUSING RECURRENT EMBOLIC STROKE UNDER ENOXAPARIN TREATMENT: DIAGNOSIS USING ULTRAFAST CARDIAC COMPUTERIZED TOMOGRAPHY (CT)**

S. Sabatay, Y. River, A.R. Zeina, D. Shari, S. Tov, A. Mahagney, B. Weller

1Department of Neurology, 1Department of Radiology, MAR Imaging Institute, Coronary Care Unit, Bnai Zion Medical Centre, Haifa, Israel

Atrial myxoma represents a rare but important cause of stroke, usually affecting young people. The ultrafast cardiac CT represents a non-invasive, rapid option in diagnosing intracardiac masses in patients with suspected embolic strokes. We report a 69-year-old woman who presented with mild dysarthria, right internuclear ophthalmoplegia and a mild left hemiparesis. Brain CT performed at admission revealed small lacunar infarcts in the basal ganglia and the patient was started with subcutaneous Enoxaparin 60 mg bid. Trans-oesophageal ultrasound of the heart and ultrafast cardiac CT showed the presence of a mobile atrial myxoma attached to the annulus of the posterior mitral leaflet, protruding through the mitral orifice. 3 days following admission a right arm paresis was noticed on neurological examination and the patient was urgently transferred to the cardiovascular surgery unit where removal of the myxoma was performed. The macroscopic examination revealed a friable myxoma. Following surgery the patient was stable, without any additional embolic events for a period of a 3 months follow-up.

**Conclusion:** Stroke is the most frequent clinical presentation of atrial myxomas. Ultrafast cardiac CT is evolving as an additional reliable, non-invasive, and rapid tool for diagnosing intracardiac masses, together with echocardiography. The recurrence of stroke, in spite of Enoxaparin treatment, shows that surgical excision is the sole management available for atrial myxomas, causing embolic stroke, irrespective of the time of stroke. We discuss the dilemma of early versus postponed cardiac surgery in patients presenting with cardio-embolic stroke secondary to atrial myxomas.

### P2041

**ANAEMIA AS A RISK FACTOR OF CEREBROVASCULAR DISORDERS IN FEMALES IN THE ARAL REGION**

G. Shamuratova, Z.R. Ibadullaev

1Department of Neurology, Tashkent Medical Academy, Tashkent, Uzbekistan

The given research was carried out in an environmentally unfavourable region of Aral – in Khorezm oblast where the greatest share of population is suffering from iron-deficient anaemia (IDA). Over 3 years 105 of potentially suffering women were examined by a method of cohort analysis (the average age was 43.5±4.8). Despite taking iron preparations they had low levels of haemoglobin. In addition, 110 females without IDA (the average age was 48.2±5.2) have been examined and which formed the control group. Clinical demographic parameters in both groups were matched. All the examinees underwent rheoencephalography and computer tomography of the brain. These investigations were conducted 2–3 times within a 2-months period of observation. It was established that a low content of haemoglobin in the blood was a risk factor in cerebrovascular disorders. Transitory ischemic attacks, cognitive disturbances, progressive neurological symptoms were more often reliably revealed in females potentially suffered from IDA as compared with the control group. Atrophy of cortical structures on computer tomogram of the brain, cerebral hypoperfusion on ultra-sound dopplerography and rheoencephalography were detected more often reliably in IDA patients than in the control group. Structural updates in cerebral tissue we related to a stable haemic and tissual hypoxia that led to local and diffuse ischaemias in cerebral tissue. Therefore, it should be considered that iron-deficient anaemia is a risk factor of cerebrovascular disturbances in women. We supposed that prevention of IDA in females could have a substantial effect on risk of developing cerebrovascular disorders.

### P2042

**RELATIONSHIP BETWEEN STROKE SEVERITY (NIHSS) AND DYNAMIC EVALUATION OF THE VASCULAR AND PLATELET HEMOSTASIS**

L.A. Shchepankevich, P.I. Pilipenko, I.V. Pikalov

1Department of Clinical Neurology and Algology, Postgraduate Faculty, Novosibirsk State Medical University, 1Department of Clinical Laboratory Diagnostic, Novosibirsk State Medical University, Novosibirsk, Russia

**Background and aim:** The platelet and vascular haemostasis are important in the pathogenesis in acute ischemic stroke (AIS). We supposed that stroke severity can be associated with haemostasis changes. The aim of this study was to evaluate the parameters of vascular and platelet haemostasis during the (AIS) and to assess the relationship with clinical stroke severity.

**Material and methods:** We prospectively enrolled 53 patients with acute ischemic stroke, and 42 consecutive healthy individuals. The plasma concentrations of β-thromboglobulin (β-TG), platelet factor-4 (PF4) and activity von Willebrand factor (vWF) were performed by the ELISA method at the onset and after 21st day of the onset of acute ischemic stroke. Stroke severity was estimated according to the National Institutes of Health Stroke Scale (NIHSS) on admission and on 21st day of AIS. We assessed the association of haemostasis changes with the NIHSS.

**Results:** Plasma activity of vWF in acute period of stroke was significantly higher than in the healthy control (120±12.5%, 101.7±1.3 accordingly p<0.05). No significant changes were observed in concentrations of β-TG (p<0.12) and PF4 (p<0.4). On the 21st day of AIS the activity of vWF, concentrations of β-TG and PF4 were significantly increased (p<0.001). We found the association between the level of vWF and stroke severity (NIHSS) p=0.023.

**Conclusions:** The activation of haemostasis as expressed by the high activity of vWF are associated with stroke severity. These changes may have an important role in the pathogenesis of stroke and effect on the stroke severity.
P2043
ONSET OF STROKE RELATED SEIZURES
A. Sieben1, Ph. Vanwalleghem1, G. Van Maele1, J. De Reuck1
1Department of Neurology, 2Department of Medical Statistics, University Hospital Ghent, Belgium

Background: Although most late-onset seizures appear within 2 years after stroke, some of them occur much later and their characteristics are unknown.

Purpose: To compare the characteristics of patients with very late-onset seizures (VLS) to those with early- (ES) and those with late-onset seizures (LS).

Patients: 204 patients with stroke-related seizures (29 ES, 128 LS and 47 VLS).

Results: Intracranial haemorrhage was a more frequent cause of ES than of LS and no cause at all of VLS. On the other hand, 25% of the VLS were related lacunar strokes. Status epilepticus occurred in 20.7% of ES, 11.7% of LS and 2.1% of VLS. Seizure recurrence was 13.8% in the ES, 54.7% in the LS and 34.0% in the VLS group. Neurological impairment, at stroke onset, and the degree of disability were more severe in patients with ES compared to those with LS and were very mild in the VLS group. The EEG findings as a whole did not show significant differences between the 3 groups, although a normal EEG was more frequent in the VLS group.

Conclusion: VLS occur in patients with minor ischaemic strokes with good recovery and a benign disease course.

P2044
JUVENILE ISCHEMIC STROKE: THE EXPERIENCE OF A STROKE UNIT
L. Tancredi1, S. Vidale1, R. Sterzi1, M. Arnaboldi1
1Department of Neurology, Ospedale S. Anna, 2Department of Neurology, Ospedale Niguarda Ca’ Granda, Como, Italy

Background and aims: It is estimated that over 10% of patients with ischemic stroke are younger than 55 years. The aim of the study was to analyze the clinical characteristics, stroke type and etiology in young people in our ward and to evaluate if clinical approach and patient outcome are modified by the actual approach of ischemic stroke.

Methods: We included patients with ischemic stroke, aged 16 to 44 years, admitted to our hospital between 2000 and 2005. Clinical data (including risk factors, diagnostic algorithm, Toast and Barnett classification, treatment) were retrospectively collected from the Stroke Unit medical records and included in a computerised database. Follow-up assessments were performed by review of medical reports.

Results: We identified 54 patients (M/F 1.16), mean age 36.5. The frequency of stroke increases with ageing; females are more prevalent in younger patients. Atherosclerotic risk profile is present (46% with one or more risk factors) and more frequently observed in people from developing countries (10%). Previous stroke or TIA is rare. The etiology often remains unknown (19%). The functional outcome is favourable (70%) despite clinical presentation at onset. 15% underwent percutaneous closure of patent foramen ovale. None died.

Conclusion: Despite extensive methods of screening, including genetical and haematological analysis, the percentage of stroke of undetermined cause is still relevant. It is difficult to interpret the role of cardiopathies at low-uncertain embolic risk and minor coagulation abnormalities. Uncontrolled and multiple risk factors remain an important cause of stroke in the described population.

P2045
EFFECT OF AMINO GUANIDINE ON BRAIN EDEMA AND BLOOD BRAIN BARRIER PERMEABILITY IN A TRANSIENT MODEL OF FOCAL CEREBRAL ISCHEMIA
A. Vakili, F. Hosseinzadeh, M. Zahedi Khorasani
Department of Physiology, Medical School, Semnan University of Medical Sciences, Semnan, Iran

Background and purpose: Pervious studies mainly focused on effect of aminoguanidine (AG) on late phase of ischemic injuries in various models of cerebral ischemia. However, effects AG on cerebral oedema and blood brain barrier (BBB) permeability have not yet been investigated in the transient model of focal cerebral ischemia.

Methods: Under chloral hydrate anesthesia, transient focal cerebral ischemia was induced in rats by 60 minutes middle cerebral artery occlusion, followed by 23 hrs reperfusion. Infarct volume, BBB permeability and brain oedema were assessed by 2,3,5-triphenyl tetrazolium chloride staining, Evans blue and dry-wet methods, respectively.

Results: Treatment with AG at doses 75, 150 and 300 mg/kg ip that given at beginning of ischemia significantly reduces infarct volume by 45%, 60% and 32%, respectively (p<0.001). Administration of AG (150 mg/kg ip) at the beginning of MCAO, significantly reduced the post-ischemic increase of brain water content (80.2±0.38% vs. 82.9±0.36%), while AG at dose 75 and 300 mg/kg did not significantly affect (81.4±0.32% and 81.5±0.5% vs. 82.9±0.36%, respectively). Moreover, treatment with AG (150 mg/kg ip), given at beginning of ischemia, reduces by Evans Blue (EB) extravasations into ischemic brain 52%, in comparison of saline group (0.49±0.06 vs. 0.94±0.13 µg/g tissue; p<0.001). Conclusion: Our findings indicate that administration of AG in early phase of transient focal cerebral ischemia reduces not only infarct volume but also brain oedema and blood-brain barrier disruption.

P2046
CEREBRAL BLOOD FLOW IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
M.M. Odinak1, A.V. Semenov1, S.Yu. Golokhvastov1, T.N. Pirskaya1, L.A. Voznyuk1
1Department of Neurology, Medical Military Academy, ‘The City Rheumatology Centre, St. Petersburg, Russia

Background: Neurological symptoms of CNS lupus lesion can be explained by cerebral blood flow disturbances and blood-brain barrier impairment. The majority of patients had repeated cerebral ischemic events. Transcranial dopplerography and Duplex ultrasonography are mobile and easy for cerebral blood flow examination.

Purpose: The evolution study of the cerebral blood flow parameters in SLE-patients with “CNS” lesion.

Methods: Clinical, magnetic resonance imaging and serologic studies were performed on 30 patients with verified diagnoses of systematic lupus erythematosus. These patients were under our supervision for 5 years. In all cases patients underwent complete extra- and transcranial Doppler of the cerebral circulation using the standard protocol (R. Aaslid).

Results: Some main results of a quality/quantity estimation of the Doppler spectra in patients with SLE have been found. Increase of an anacrot-period of systolic phase (index growing of
pulse wave rising) of more than 0.18sec. The frequency of this pattern in these patients is 56%. In 41% of investigations stenotic increase of linear velocities of blood flow in the extracranial (12%) and intracranial (29%) artery were revealed. In 24% – stenoses in M1 segment of medial cerebral artery was on both sides. Under our supervision the quantity of stenoses for the 5-years period increased. Changes of the cerebral vasoreactivity in patients with SLE were noticed (74%).

**Conclusion:** The cerebral blood flow pathology in patients with SLE is permanent and progredient.

P2047

**OCCURRENCE OF METABOLIC DISORDERS AMONG PATIENTS WITH ACUTE ISCHEMIC STROKE**

M. Wisniewska, W. Nyka

*Adults Neurology Department, Medical University of Gdańsk, Gdańsk, Poland*

**Objectives:** Metabolic disorders such as metabolic syndrome (MS), diabetes mellitus (DM), hyperlipidemia are risk factors of vascular diseases including stroke. MS is defined as the presence of abdominal obesity and at least two of the following: hypertension, hyperglycaemia, dyslipidemia- elevated triglycerides (TG), low HDL-cholesterol (HDL-ch). We aimed to evaluate the prevalence of MS, DM and hypertension among a population of patients with acute ischemic stroke.

**Methods:** Research assessed 100 patients, 53 female (F), 47 male (M) aged from 41 to 92 (mean age 71.6±10.6) from the Stroke Department, Medical University of Gdańsk, hospitalized between 2005 and 2007. MS was recognized according to definitions of National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII), International Diabetes Federation (IDF), American Heart Association-National Heart, Lung and Blood Institute (AHA-NHLBI). The cerebral blood flow pathology in patients with SLE are related with men, women are older (73.0 yrs. vs. 68.9 p<0.001) and had more frequent atrial fibrillation (42.9% vs. 20.0% p<0.003); coronary heart disease (56.1% vs. 43.5% p<0.017); but smoking (35.8% vs. 25.6) and intense alcohol consumption (28.2% vs. 1.02% p<0.001) were more frequent in men. Other differences in risk factors were not found. Neurological deficits were more intensive in women, not only at admission SSS (32.1 vs. 39.5 p<0.001), but also at discharge SSS (43.0 vs. 48.3 p<0.03). Women were also more dependent at discharge (BI 58.6 vs. 76.5 p<0.02). Deaths were frequent in the women population (23.4% vs. 17.4%).

**Conclusions:** The study showed significant sex differences in frequency of risk factors, clinical picture and stroke outcome. Clinical course of stroke in female patients was more severe and outcome was less optimistic.

P2049

**LOCAL INFLAMMATION FACTORS AND ASSESSMENT OF NSAIDS EFFICACY IN THE TREATMENT OF CEREBRAL HAEMORRHAGE**

M.M. Asadullayev¹, F.S. Saidvaliyev², U.M. Asadullayev³

¹Neurological Department, Tashkent Medical Academy, Tashkent, Uzbekistan

**Methods:** We analyzed 183 consecutive patients admitted due to ischemic stroke. The patients were classified according to Oxfordshire and TOAST. Severity of neurological deficits was assessed using Scandinavian Stroke Scale (SSS) and independence with Barthel index (BI). The cerebral blood flow pathology in patients with SLE is permanent and progredient.

P2050

**THE RELATIONSHIP BETWEEN HELICO BACTER PYLORI-INFECTION AND THROMBOTIC ISCHEMIC STROKE**

F. Ashtari, V. Shaygannejad, A. Saberi, E. Rabiee

Neurology Ward, Alzahra Hospital, Esfahan Medical and Research University, Esfahan, Iran

**Conclusion:** The study shows that MS is more prevalent among women compared to men with stroke. Women more often suffer from abdominal obesity and hypertension. There is also higher frequency of elevated total cholesterol and LDL-ch among women. Elevated TG and low HDL-ch is more prevalent among men.

P2048

**GENDER DIFFERENCES IN ISCHEMIC STROKE. THE ANALYSIS OF THE CLINICAL PICTURE, RISK FACTORS AND OUTCOME**

E. Strozynska¹, U. Fiszer², J. Zaborski¹

¹Department of Neurology and Neurorehabilitation, Miedzyleski Szpital Specjalistyczny W Warszawie, ²Klinika Neurlogii I Epileptologii, CMKP W Warszawie, Warsaw, Poland

**Background:** Previous studies have documented differences in patients with cardiovascular disease. However, little data exist on whether similar sex differences exist in stroke patients. The study sought to investigate gender-related differences in patients with acute stroke.

**Methods:** We analyzed 183 consecutive patients admitted due to ischemic stroke. The patients were classified according to Oxfordshire and TOAST. Severity of neurological deficits was assessed using Scandinavian Stroke Scale (SSS) and independence with Barthel index (BI).

**Results:** Women predominated in the study group (53.3%). Compared with men, women were older (73.0 yrs. vs. 68.9 p<0.001) and had more frequent atrial fibrillation (42.9% vs. 20.0% p<0.003); coronary heart disease (56.1% vs. 43.5% p<0.017); but smoking (35.8% vs. 25.6) and intense alcohol consumption (28.2% vs. 1.02% p<0.001) were more frequent in men. Other differences in risk factors were not found. Neurological deficits were more intensive in women, not only at admission SSS (32.1 vs. 39.5 p<0.001), but also at discharge SSS (43.0 vs. 48.3 p<0.03). Women were also more dependent at discharge (BI 58.6 vs. 76.5 p<0.02). Deaths were frequent in the women population (23.4% vs. 17.4%).

**Conclusions:** The study showed significant sex differences in frequency of risk factors, clinical picture and stroke outcome. Clinical course of stroke in female patients was more severe and outcome was less optimistic.

P2051

**COGNITIVE IMPAIRMENT AND RAPIDLY EVOLVING LEUKOARAIOSIS IN ISCHEMIC STROKE PATIENTS PREDICTED BY EARLY CEREBRAL SPECT HYPOPERFUSION**

D.C. Marinescu, O.A. Bajenaru

Neurology Department, University Emergency Hospital, Bucharest, Romania

**Conclusion:** The cerebral blood flow pathology in patients with SLE is permanent and progredient.
P2053
SEIZURE AS THE FIRST MANIFESTATION OF A COMPLEX CEREBROVASCULAR DISEASE
L. Dezmalj Grbelja, J. Bosnjak, R. Covic Negovetic, A. Huzjan Lovrencic, V. Demarin
University Department of Neurology, University Hospital Sestre Milosrdnice, Zagreb, Croatia

P2054
THE EVALUATION OF ENDOTHELIAL DYSFUNCTION IN DIFFERENT SUBTYPES OF ACUTE ISCHEMIC STROKE
1Acute Stroke Department, Institute of Neurology, 2Laboratory of Hemorheology and Hemostasis, Institute of Neurology, RAMS, Moscow, Russia

P2055
CLINICAL AND IMMUNE FEATURES IN PATIENTS AFTER STROKE
M. Gerasimova, A. Evdokimov
Tver State Medical Academy, Tver, Russia

P2056
PATHOPHYSIOLOGIC MECHANISMS OF VERTEBRO-BASILAR INSUFFICIENCY
M. Gerasimova, L. Fomina
Tver State Medical Academy, Tver, Russia

P2057
THE ROLE OF CONNECTIVE TISSUE DESTRUCTION IN PATHOGENESIS OF CEREBRAL HEMORRHAGE
M. Gerasimova, O. Pogoreltseva
Tver State Medical Academy, Tver, Russia

P2058
Abstract cancelled

P2059
AN ETIOLOGIC STUDY OF CEREBRAL VASCULAR ISCHEMIC EVENTS IN YOUNG ADULTS IN ARDABIL (IRAN)
M. Hashemilar, D. Savadi Oskoyi, M. Jafariani, A. Abedi, N. Amin Sami
1Department of Neurology, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, 2Department of Neurology, Tabriz University of Medical Sciences, Tabriz, 3Faculty of Medicine, University of Medical Sciences, Tabriz, 4Faculty of Medicine, University of Medical Sciences, Ardabil University of Medical Sciences, Ardabil, Iran

P2060
VASCULAR AGE IN SMOKERS
M.J. Jurasic, S. Morovic, R. Sarac, V. Demarin
1University Department of Neurology, Sestre Milosrdnice University Hospital, 2Special Hospital for Pulmonary Diseases, Zagreb, Croatia

P2061
TWO CASES OF RECURRENT STROKE ILLUSTRATING MTHFR-MUTATION AS AN INDEPENDENT RISK FACTOR, WITH RESISTANCE TO VITAMIN THERAPY
G. Laureys, S. Gheuens, V. Bissay, G. Ebinger, A. Michotte
Department of Neurology, UZ Brussel, Belgium

P2062
18 MONTHS FOLLOW-UP OF PATIENTS WITH VASCULAR COGNITIVE IMPAIRMENT TREATED WITH DONEPEZILE
A. Rossiniol-Far, J. Llinas-Servera
Fundacio Per L’Avanç de Les Neurociencies, Palma de Mallorca, Balearic Islands, Spain

P2063
CERUM LEUCOCYTE COUNT ON ADMISSION AS PREDICTORS OF VASOSPASM SEVERITY AND OUTCOME AFTER SAH
N.N. Lobjanidze, L.Z. Bakradze, A.D. Jeiranashvili
1Department of Neurology, 2Department of Neurosurgery, Georgian State Medical University #2 Clinic, Tbilisi, Georgia

P2064
CLINICAL, IMAGISTIC AND LABORATORY ASPECTS IN ACUTE ISCHEMIC STROKE
I. Macavei, A. Macavei, I. Macavei, R. Suciu, T. Bara
1Department of Neurology, University of Medicine and Pharmacy, 2University of Medicine and Pharmacy, 3Department of Surgery, University of Medicine and Pharmacy, Tirgu Mures, Romania

P2065
THE CORRELATION BETWEEN CLINICAL AND NEUROIMAGISTIC ASPECTS OF INTRACEREBRAL HEMORRHAGE
A. Macavei, I. Macavei
Department of Neurology, University of Medicine and Pharmacy, Tirgu Mures, Romania

P2066
SOME ASPECTS OF THE TREATMENT OF CEREBELLAR HEMATOMAS: A SMALL RETROSPECTIVE STUDY
S. Aphridonidze, E. Melikidze, M. Megrelishvili, M. Janelidze, R. Shakarishvili, A. Gvelesiani, N. Akashvili, R. Lukava
1Department of Neurology, 2Department of Neurosurgery, Tbilisi State Medical University, Tbilisi, Georgia

P2067
FREQUENCY, RISK FACTORS AND OUTCOME OF LACUNAR INFARCTIONS
S. Miljkovic, D. Racic, M. Arbutina, Z. Vujkovic
Department of Neurology, University Clinical Centre Banjaluka, Banjaluka, Bosnia-Herzegovina
P2068
SOME METABOLIC DYSFUNCTION IN PATIENTS WITH LACUNAR STROKE
I.D. Pashkouskaya, N.I. Nechipurenko, L.N. Anatskaia, T.V. Griboeidova
Belarusian Research and Practical Centre of Neurology and Neurosurgery, Minsk, Belarus

P2069
MOYA-MOYA DISEASE
V.V. Ponamaryov1, O.A. Udina2
1Neurological Department, Hospital, 2Minsk, Belarus

P2070
THE ROLE OF EARLY PHYSICAL THERAPY IN PREVENTION OF COMPLICATIONS IN PATIENTS WITH STROKE
D. Okiljevic1, S. Popovic1, A. Radosavljevic1, R. Raicevic1
1Department of Physiatry, 2Department of Neurology, 3Department of Radiology, Military Medical Academy, Belgrade, Serbia

P2071
AUTO EXPANDABLE STENTS IN THE TREATMENT OF INTRACRANIAL SYMPTOMATIC ATHERSCLEROTIC STENOSIS
R. Rangel Guerra1, A. Garcia De La Fuente2
1Centro De Especialidades Medicas, Monterrey, 2Hospital Christus Muguerza, Nuevo Leon, Mexico

P2072
ACUTE STROKE - ATRIAL MYXOMA
P.N. Renjen
Department of Neurosciences, Indraprastha Apollo Hospitals, New Delhi, India

P2073
MANNITOL TREATMENT IN STROKE PATIENTS IN A PROSPECTIVE, OBSERVATIONAL STUDY PERFORMED DURING 1 YEAR IN TARGU-MURES EMERGENCY HOSPITAL, ROMANIA
I. Szocs1, K. Orban-Kis2, J.A. Szasz2, Z. Bajko2, K. Fekete2, Sz. Szatmari1
12nd Clinic of Neurology, Targu-Mures Emergency Hospital, 2Department of Physiology, 3Department of Neurology, University of Medicine and Pharmacy Targu-Mures, Targu-Mures, Romania

P2074
EMOTIONAL SYMPTOMS IN ACUTE ISCHEMIC STROKE
V. Vuletic1, M. Ratkovic-Lozert1, L. Sapina1, Z. Lezaic1, M. Bitunjac2
1Department of Neurology, 2General Hospital, Slavonski Brod, Croatia

P2075
DEPRESSIVE SYMPTOMS AND STROKE OUTCOME
I. Zavoreo1, N. Blažič Čop2, V. Demarin3
1Neurology Department, UH Sestre Milosrdnice, Zagreb, Croatia

Ageing and dementia 2

P2076
NEURONAL CULTURES DERIVED FROM MOUSE EMBRYONIC STEM CELLS AS MODELS FOR NEURO-DEGENERATIVE DISEASES
B.A. Bergmans1, A. Herreman1, L. Serneels1, S.S. Hebert, B. De Strooper
Laboratory for Neuronal Cell Biology and Gene Transfer, Department of Molecular and Developmental Genetics, VIB, KU Leuven, Belgium

Neurons are an essential source of material to study the different aspects of neurodegeneration. However, the use of primary neuronal cultures has its limitations (e.g. low yield, high costs, etc.). Also, neuronal cultures cannot be generated from knockout mice which display embryonic lethal phenotypes. A nice alternative is the generation of neurons derived from embryonic stem (ES) cells. Our objective is to obtain high-purity neuron cultures derived from mouse ES cells to study the contribution of genes involved in Alzheimer’s disease (AD) to neurite outgrowth, synapse formation and neuronal cell death. The differentiation protocol by Bibel et al. (Nat Neurosci 7 (2004):1003-1009) was used to obtain highly pure cultures of glutamatergic pyramidal neurons from mouse ES cells. Assessment of neuronal purity, neuronal differentiation and establishment of neuronal polarity was performed by immunofluorescence using the neuronal marker TUJ1 and the axonal and dendritic markers Tau and Map2. To study synaptic contact formation, we also investigated Synaptophysin expression patterns. Our results indicate that mouse ES cells can differentiate into hippocampal-like neurons. This could be reproduced with ES cells derived from AD-related ApoE KO mice. We show that neurons derived from mouse ES cells could be a useful and reliable alternative to primary hippocampal cultures for studying neurite outgrowth, synapse formation and many other processes thought to be disrupted in neurodegenerative diseases such as AD. B.A.B. is a Research Assistant of the Fund for Scientific Research Flanders

P2077
CLINICAL WORSENING DESpite VARIOUS IMMUNOTHERAPY IN HASHIMOTO-ANTIBODIES ASSOCIATED WITH ENCEPHALOPATHY
J.C. Bier1, H. Slama2, S. De Breucker1, L. Victor2, M. Vokaer1
1Department of Neurology, 2Department of Neuropsychology, 3Department of Geriatry, Erasme Hospital, Brussels, Belgium

Background: First description of a “Steroid-Responsive Encephalopathy Associated with autoimmune Thyroiditis (SREAT)” syndrome dated 1966. Since then, lots of cases emerged with two major kinds of presentation: “vasculitic” and “diffuse progressive”. Patients respond variably to corticoids. Methotrexate, plasmatic exchange or intra-venous immunoglobins (IvIG) have only been anecdotically used.

Case report: A 63-year-old man came in 2000 complaining of difficulty finding easy words while speaking for past 5 years. He lost appetite and was tired despite sleeping 10 hours/day for 3 years. He presented bradypsychia and MMSE was 28/30. Diagnosis of depression was proposed and treated. At this time, he went to sleep while eating or watching TV. EEGs and usual blood investigations were normal. During the next 3 years, he presented left extinction and extra-pyramidal gait followed by spontaneous myoclonus.
Both lumbar puncture and brain MRI were normal despite atrophy. Diagnosis of cortical posterior atrophy due to possible corticobasal degeneration was then set up. Cognitive decline rapidly progressed and anti-TPO antibodies were positive at >3000 UI/ml. Treatment by oral methylprednisolone (64 mg/day during 1 month) was initiated and then followed by a delirious major depressive disorder requiring hospitalization. Over the next years, cognitive decline persisted and treatments by methylxtrate, prednisolone and even IV Ig were all followed by worsening of myoclonus and psychosis relapses.

Conclusions: This case of clinical worsening after immunotherapy highlights the necessity to cautiously study the response of SREAT to immune-therapies.

P2078
STUDY OF SERUM LIPOPROTEIN PROFILE AND APOE GENOTYPE IN ALZHEIMER’S DISEASE.
A. Cagnin¹, A. Zambon², G. Zarantonello¹, D. Vianello¹, D. Mercurio¹, F. Miccichè², A. Stecca¹, V. Lunardelli¹, A. Leon¹, L. Battistin¹•

¹Department of Neuroscience, ²Department of Internal Medicine, University of Padova, ³Department of Research and Innovation, Padova, IRCSS Ospedale San Camillo, Venezia, Italy

Background: Alterations in cholesterol homeostasis are associated with Alzheimer’s disease (AD). The role played by specific fractions of serum lipoproteins in modifying the risk of AD, and the interaction with APOE genotype, has not yet been investigated.

Objective: To study the serum lipoprotein profiles in a cohort of late-onset sporadic AD patients without cerebrovascular lesions and in healthy elderly subjects.

Methods: 50 patients with sporadic late-onset AD and 60 healthy elderly controls were studied. Each subject underwent an extensive clinical work-up including neuropsychological assessment and MRI brain imaging. Serum concentrations of lipoproteins were measured by a gradient-density ultracentrifugation method. Apolipoprotein E genotyping was also performed.

Findings: In the AD group the lipoprotein cholesterol distribution showed increased total cholesterol and LDL cholesterol, reaching a significant difference in respect to controls in those LDL subfractions representing the transition between small dense-LDL (sd-LDL) and normal-density LDL particles (p<0.05). APOE genotype and LDL cholesterol were independently associated with AD. The mean concentration of sd-LDL increased the risk of developing AD (p<0.05).

Conclusion: These results confirm that alteration of cholesterol homeostasis is associated with AD and that serum concentration of LDL cholesterol is higher in AD than in normal elderly subjects, also in those patients without cerebrovascular pathology. The presence of APOE e4+ allele is a risk factor for AD independent of an increased level of serum cholesterol. Increased levels of specific sub-fractions of LDL cholesterol may be associated with increased risk of AD.

P2079
THE PROGRESSIVE ACCUMULATION OF NFTS COMPOSED OF D421 AND E391 CLEAVED TAU CORRELATED WITH THE NEUROPATHOLOGY AND CLINICAL SEVERITY OF ALZHEIMER’S DISEASE
E. García-Sierra¹, G. Basurto-Islas¹, N. Barragán¹, J. Luna-Muñoz¹, A.L. Guillózet-Bongaarts¹, R.W. Berry¹, L.I. Binder¹, R. Mena³

¹Department of Cell Biology, ²Department of Neuroscience, Centre of Research and Advanced Studies, The National Politehnical Institute, Mexico City, Mexico, ³Department of Cell and Molecular Biology, North-western University Medical School, Chicago, IL, USA

In Alzheimer’s disease (AD), truncation of tau protein at E391 is an important modification involved in the formation of paired helical filaments and NFTs. Also, the caspase product D421 cleaved tau, has been found associated with NFTs, however the clinical significance of NFTs carrying both truncation has been poorly analyzed in AD. In this study, in a population of 40 AD and control cases, we analyzed and compared by immunohistochemistry the progression of NFTs composed of D421 versus E391-truncated tau in relation to clinical and neuropathological parameters of the disease. NFTs recognized by Tau-C3 and MN423 were observed during the initial stages of AD in areas associated with the perforant pathway. The total density of NFTs correlated significantly with the Braak staging (BST) and the clinical severity of dementia (CAMDEX) (r=0.6122, p≤0.001; and r=0.5051, p=0.0009, respectively). The same correlations were found for NFTs composed of E391 truncated tau (immunoreactive to MN423) (r=0.634, p≤0.0001; and r=0.5149, p=0.0007, respectively), however we found an inverse distribution of NFTs recognized by either Tau-C3 or MN423 along the major areas of the perforant pathway. Our results indicate that accumulation of NFTs composed of D421 and E391 truncated tau significantly correlates with clinical severity of dementia. However, they display different profiles of distribution along allocortical areas. Our results also indicate D421 truncation may precede and facilitates the appearance of advanced E391 cleavage of tau in NFTs.

P2080
SEVERITY OF DEMENTIA IN ALZHEIMER’S DISEASE DEPENDS ON IGF-1 LEVEL BUT NOT ON IGF-1 PROMOTER POLYMORPHISM
A.M. Geppert¹, M. Koczorowska¹, A. Godzicka-Jozefiak², E. Przedpelska-Ober³

¹Department of Neurology, University of Medical Sciences, Poznan, ²Department of Molecular Virology, Institute of Molecular Biology and Biotechnology, Poznan, Poland

Insulin-like growth factor 1 (IGF-1) is involved in the regulation of cell proliferation and differentiation acting as neuroprotector. Detailed evidence demonstrates that Alzheimer’s disease (AD) and especially advanced AD Braak stages are associated with progressively reduced levels of IGF-1 in the brain. Since IGF-1 was established as responsible for protection against neuronal death and loss of synapses, IGF-1 was a target factor in our searching for the influence on disease progression. The main purpose was to analyse serum levels of IGF-1 and IGFBPs in patients with demencing diseases, and to correlate both factors with clinical markers of disease progression represented by MMSE and GDS.

Our scientific interest covered as well the polymorphism of IGF-1 promoter region as possible pathology influencing the functional role of this protein. In the first step, a population of 100 patients including 53 patients with dementia and 47 patients with other neurological disorders than dementia were investigated in the study. IGF-1 and IGFBP-3 serum levels were determined using ELISA Kit. Polymorphism of IGF-1 promoter region was analyzed with PCR and SSCP reactions. Discovered dependencies between higher IGF-1 level and higher MMSE score confirmed protective effect of IGF-1 on the severity of dementia in AD patients. Investigation of IGF-1 promoter region polymorphism was negative but showed the same point mutation in 2 patients with LOAD. The significance of our result has a therapeutic aspect. Our present observation of protective IGF-1 influence may be the basis for the further development of the new treatment – prevention of AD progression.
P2081
HIGH PREVALENCE OF THYROID DYSFUNCTION IN A MIXED MEMORY CLINIC POPULATION
A. Heij1, K. Phung1, B.B. Andersen1, U. Feldt-Rasmussen1, G. Waldemar1
1Memory Disorders Research Unit, Department of Neurology, 2Department of Endocrinology, Rigshospitalet, Copenhagen, Denmark

Background and aims: Memory impairment may be the first sign of Alzheimer’s disease, but not every case represent an irreversible degenerative dementia disorder and some reversible conditions may cause or mimic dementia. The aim of this study was to investigate the prevalence of thyroid disease in a prospective memory clinic cohort of younger and elderly patients with cognitive symptoms.

Methods: The study included the primary analysis of 2,296 consecutive patients referred during a period of 86 months to a university hospital multidisciplinary memory clinic based in neurology. All patients were referred for diagnostic evaluation and treatment of cognitive symptoms. As part of the diagnostic evaluation laboratory screening tests were performed in all patients.

Results: The mean age of the patients was 67 years (range 17–98) and the frequency of women was 54%. Abnormal thyroid stimulating hormone (TSH) was found in 9.8% of all patients; 4.2% had increased level of TSH suggesting hypothyroidism and 5.6% had reduced TSH indicating hyperthyroidism.

Conclusion: We found a high frequency of TSH abnormalities in a mixed cohort of memory clinic patients. Hyperthyroidism as well as hypothyroidism may contribute to cognitive impairment as comorbidity in dementia, or may represent the main cause of mild subjective cognitive symptoms.

P2082
TARENFLURBIL (MPC-7869, FLURIZAN), A SELECTIVE 12-MONTH PHASE-2 TRIAL
S. Hendrix1, J. Mintzer1, K. Zavitiz1, M. Laughlin1
1Myriad Pharmaceuticals, Salt Lake City, UT, 2Department of Psychiatry, Medical University of South Carolina, Charleston, SC, USA

Background: Tarenflurbil is a Selective Ab42-Lowering Agent (SALA) that lowers brain levels of Ab42 in a mouse model of AD and chronic dosing in this model prevents defects in learning and memory. These data and the Phase-2 study indicating sustained benefit in activities of daily living, global function and cognition in mild AD patients, suggest the potential for tarenflurbil to have disease-modifying properties.

Methods: This was a placebo-controlled, 1-year study evaluating tarenflurbil in 207 patients with mild-to-moderate AD. At randomization, 94% of subjects were on stable acetylcholinesterase inhibitor therapy. An exploratory post-hoc analysis was performed which compared the time to adverse psychiatric events between treatment groups.

Results: In subjects with mild AD (MMSE 20–26) was a significant delay in time to clinically significant adverse psychiatric events, 800 mg BID compared to placebo (p=0.011). Among 35% of the placebo group who had an event, the median time was approximately 106 days. In the 800 mg BID group, the median time to event was greater than 333 days with only 14% of this group having an event. The most common psychiatric events reported in the placebo group were agitation, aggression, confusional state and depression.

Conclusion: In addition to the reported significant benefit observed in activities of daily living (p=0.033) and global function (p=0.042), this analysis revealed a significant delay in time to psychiatric events. These results are consistent with the hypothesis that treatment with tarenflurbil may delay progression of AD.

P2083
AGE-ASSOCIATED IMBALANCE BETWEEN DAT AND VMAT-2: A POSSIBLE MECHANISM OF INCREASED SUSCEPTIBILITY TO MPTP TOXICITY IN AGED C57BL/6N MICE
Y.B. Cheng1,2, J.J. Qiang1, C.F. Liu2, W.D. Hu1, K.Y. Liu1,2, C.J. Mao1,2
1Department of Neurology, Second Affiliated Hospital of Soochow University, 2Laboratory of Aging and Nervous Diseases, Soochow University, Suzhou, China

Background and aims: There are lots of evidences showing an increased susceptibility to neurotoxins in aged animals, but the mechanism remains elusive. To investigate the age-related alterations of DAT and VMAT-2 and the potential correlations with increased susceptibility to MPTP in aged mice.

Methods: In the present study, we produced 4 groups of different ages (3, 9, 16 and 24 months old) C57BL/6N mice. The expression level of DAT and VMAT-2 in striatum was detected by western bloting and real-time PCR, and the amount of tyrosine hydroxylase positive cells was counted in serial sections of substantia nigra in different age groups both normal control and exposed to MPTP (30 mg/kg i.p. at 24 hours intervals for 5 days).

Results: DAT, VMAT-2 and amount of TH positive cells manifested an age-associated decline during normal aging, and we discover a distinct lower ratio of VMAT-2 to DAT in aged mice (16 and 24 months-old group). When treated with MPTP, the old mice lost more TH positive cells and showed a more significant decline in protein level of DAT and VMAT-2.

Conclusions: Our results indicate that the imbalance between DAT and VMAT-2 during aging may contribute to the increased susceptibility to MPTP toxicity in aged C57BL/6N mice.

P2084
CLAUDIN 11 AND CLAUDIN 2 IN ALZHEIMER’S DISEASE AND VASCULAR DEMENTIA
M.O. Romanitan1,2, B. Winblad1, O.A. Bajenaru1, N. Bogdanovic3
1Department of Neurology, Emergency University Hospital, Bucharest, Romania; 2Alzheimer’s Disease Research Centre, Karolinska Institutet, Stockholm, Sweden

The tight junctions (TJs) contain integral membrane proteins. Claudin-11 (C11) is important in the formation of myelin sheath while claudin-2 (C12) is a major structural component of TJ strands expressed by the epithelial cells. The aim of this study is to analyze C11 and C12 expression in cerebral microvasculature and frontal cortex in control ageing brains, Alzheimer’s disease (AD) and Vascular Dementia (VD). The brain material was obtained from the Huddinge Brain Bank, Stockholm. The study was based on 19 cases. Immunostaining with rabbit polyclonal antibodies against C11 and C12 was performed on paraffinmaldehyde-fixed embedded sections followed by quantitative approach using stereological principles. The neurons, astrocytes and oligodendrocytes were quantified while stained vessels were appreciated qualitatively. Both Claudins were expressed by neurons, glial cells and vessels with better expression of C11. The stained neurons were predominantly pyramidal. The endothelium was stained both in white and gray matter. In the control group, the percentage of stained
neurons and glial cells was almost three times increased for C11 compared to C12. In AD and VD there was an increase of claudins expression by neurons and glial cells compared to control cases and C11 was better expressed compared to C12. The study sustains the idea of claudin’s expression in human brain neurons, glial cells and vessels suggesting that there is an increase of claudin’s expression in the pathological conditions such as AD and VD compared to controls, more obvious for claudin-11; the findings could reveal new pathogenic pathways in dementia disorders.

P2085
THE PLASMA LEVEL OF AMYLOID B42 IS INDEPENDENT OF NEURONAL ACTIVITY IN ALZHEIMER’S DISEASE
F. Sedaghat, A. Gotzamani-Psarrakou, V. Costa, A.S. Dimitriadis, S.J. Baloyannis
AHPEA University Hospital, Thessaloniki, Greece
Amyloid β42 (Aβ42) aggregation is said to be one of the major pathogenic events in Alzheimer’s disease (AD). Regional cerebral blood flow (rCBF) studies using SPECT help the diagnosis of AD. The aim of this study is to evaluate any correlation between rCBF in different regions of the brain and plasma level of Aβ1-42 in AD. To date we have found no study concerning this. Any correlation between age and sex, with Aβ42 and rCBF was studied. 45 subjects were included in the study. 29 patients (mean age 71±9) with a diagnosis of AD fulfilled NINCDS-ADRDA criteria with a mean MMSE of 15±9, and 16 normal controls (mean age 64±8) underwent HMPAO SPECT brain imaging. Semiquantitative analysis of rCBF was done. Plasma samples were collected the same day as HMPAO SPECT. Plasma Aβ1-42 was measured using ELISA. A significant reduction of rCBF was observed in most regions of the brain in AD comparing controls. Mean Aβ42 did not differ between two groups (16.3± 15.5 pg/ml in AD, 12±7.7 pg/ml in controls). There was no correlation between rCBF in any region, and plasma levels of Aβ42 in no group. No correlation between sex and age with plasma levels of Aβ42 and rCBF was found. Since rCBF is related to neuronal activity, we conclude that plasma Aβ1-42 concentration is independent of neuronal function and can not differentiate AD from normal controls while rCBF is signific-antly reduced in AD. RCBF and plasma Aβ42 are not affected by sex and age in AD.

P2086
CEREBROSPINAL FLUID TAU PROTEIN AND AMYLOID β42 CORRELATION WITH THE NEUROPSYCHOLOGICAL EXAMINATION IN MILD COGNITIVE IMPAIRMENT AND MILD ALZHEIMER DISEASE PATIENTS
A. Speth1, C. Sindic2, X. Seron1, A. Ivanov1
1Department of Psychology, University of Louvain, Louvain-La-Neuve, 2Neurology Department, 1Memory Clinic and Neuropsychological Rehabilitation Centre, Saint Luc Hospital, Bruxelles, Belgium
Background and objective: Abnormal levels of Tau protein and Amyloid β42 (Aβ42) were found in the cerebrospinal fluid (CSF) of patients with mild cognitive impairment (MCI) and Alzheimer’s disease (AD). It is not clear if the biological changes in the CSF are correlated with the cognitive impairment. Recently, we found that a high Tau protein CSF level was correlated with low memory performance in MCI and mild AD. No significant correlation was found between the CSF level of Aβ42 and memory. The present study aim is assessing the correlation between CSF Tau protein and Aβ42 and cognitive measures in a larger group of patients.

Material and methods: 50 mild AD patients, 48 MCI patients and 22 anxious and depressed elderly patients (AnxioDep) were included. The CSF was collected by lumbar puncture. All subjects performed 9 cognitive tests assessing language, episodic and semantic memory, visuo-spatial processing, attention and executive functions.

Results: Memory measures correlated with the Tau protein level whereas the semantic fluency task was correlated with the Aβ42 level within the group including MCI and mild AD patients. A multiple backward linear regression disclosed the Tau protein, Aβ42, a measure of verbal memory and the semantic fluency task as independent predictors of the MCI status vs. AnxioDep.

Conclusions: We found significant correlations between the CSF Tau protein and Aβ42 levels and cognitive measures in MCI and mild AD. The status of MCI was predicted independently by several variables, both biological and cognitive.

P2087
DONEPEZIL STABILIZES FUNCTION IN SEVERE ALZHEIMER’S DISEASE PATIENTS
B. Winblad1, Y. Xu2, K. Albert1
1Department of Neurotec, Karolinska Institutet, Karolinska University Hospital, Huddinge, Stockholm, Sweden, 2Biometrics Department, Alzheimer’s Disease Management Team, Pfizer Global Pharmaceuticals, Pfizer Inc., New York, USA

Aim: To examine the relationship between cognitive response to donepezil and activities of daily living (ADL) in patients with severe Alzheimer’s disease (AD).

Methods: In a 6-month, randomized, placebo-controlled study of donepezil in severe AD, cognition and ADL were assessed using the Severe Impairment Battery (SIB) and the Alzheimer’s disease Cooperative Study ADL-severe (ADCS-ADL-sev), respectively. In this post-hoc analysis, the month 6 least-square mean change from baseline total score on the ADCS-ADL-sev and basic and instrumental subscale scores were analyzed for patients who showed stabilization or improvement on the SIB (COG subgroup) or a ≥4-point improvement on the SIB (HIGH COG subgroup).

Results: At month 6, for the ADCS-ADL-sev, mean change from baseline to the overall donepezil (n=109) and placebo groups (n = 107) were –1.4 and –3.0 respectively; treatment difference =1.7 (p<0.03). For the 69% (n=75) of donepezil-treated patients in the COG subgroup, mean change from baseline was 0.20; for the 57% (n=62) of donepezil-treated patients in the HIGH COG subgroup, mean change from baseline was similar at 0.22. Benefits were observed in all 6 basic ADL and 11 of 13 instrumental ADL for donepezil-treated patients in the COG and HIGH COG subgroups compared with the overall donepezil group.

Conclusion: In severe AD, donepezil decreases the degree of decline in ADL. For patients with cognitive stabilization and/or improvement, overall function is stabilized with benefits observed in 17 of 19 ADL items.

P2088
A RESPONDERS ANALYSIS OF TARENFLURBIL (FLURIZAN), A SELECTIVE ABETA42-LOWERING AGENT, IN MILD ALZHEIMER’S DISEASE: ANALYSIS OF A PHASE-2 STUDY OF UP TO 24 MONTHS
K. Zavitz, S. Hendrix, M. Laughlin, E. Swabb
Myriad Pharmaceuticals, Salt Lake City, UT, USA

Background: Tarenflurbil is a Selective Ab42-Lowering Agent (SALA) that lowers brain levels of Ab42 in a mouse model of AD and chronic dosing in this model prevents defects in learning and memory suggesting the potential for tarenflurbil to have disease-modifying properties. In subjects with mild AD (MMSE 20–26)
randomized to 800 mg BID, statistically significant benefit was observed at 12 and 24 months in activities of daily living and global function with positive trends observed in cognition.

**Methods:** This was a placebo-controlled trial evaluating tarenflurbil treatment in 207 patients with mild-to-moderate AD for up to 24 months. At randomization, 94% of subjects were on stable acetylcholinesterase inhibitor therapy. Primary outcomes were ADAS-cog, ADCS-ADL, and CDR-sb. A post-hoc responder analysis was performed in subjects with mild AD (MMSE 20–26) in which a “responder” was defined as a subject who shows improvement or no decline compared to baseline.

**Results:** 60% of subjects randomized to 800 mg BID were responders on at least one primary outcome at month 12 compared to 39% of subjects on placebo (p=0.063). At 24 months, 45% of subjects randomized to 800 mg BID were responders on at least one outcome, compared to only 11% of subjects randomized to placebo (p=0.035). These and additional analyses suggest that subjects treated with tarenflurbil show an increasing response rate over time on primary outcomes in a dose dependent manner.

**Conclusion:** These analyses further justify the ongoing Phase 3 clinical trials of tarenflurbil as an amyloid-based treatment strategy for mild AD.

**P2089**  
**SUBACUTE PROGRESSIVE DEMENTIA: A CASE-REPORT**

C. Albreten 1, O.A. Hansen 1, S. Loeseth 1, O.C. Borota 1  
1Department of Neurology, University Hospital, North-Norway, Tromsa, 2Department of Pathology, The National Hospital, Oslo, Norway

A 74-year-old woman with previous history of cervical carcinoma, kidney failure, chronic obstructive lung disease and chronic diarrhoea, was admitted to the hospital due to haematemesis and melena. Oesophageal ulcer was diagnosed. Increasing cognitive failure was observed during hospitalization. After a month she got worse and lost consciousness. CT scan revealed no sign of cerebral bleeding or infarction. Neurological examination revealed somnolence, eye deviation to the left, weak, unclear, hardly understandable speech and symmetric rigidity in upper and lower extremities. The reflexes were normal, Babinsky negative. Single, asynchronous, myoclonic movements were observed mainly in right upper limb, seldom on the left side. EEG revealed periodic sharp complexes over time on primary outcomes in a dose dependent manner.

**Conclusion:** These analyses further justify the ongoing Phase 3 clinical trials of tarenflurbil as an amyloid-based treatment strategy for mild AD.

**P2090**  
**COMPARATIVE SAFETY AND TOLERABILITY OF ALZHEIMER’S DISEASE TREATMENTS**

1ATP Clinical Research, Costa Mesa, CA, 2Forest Research Institute, Jersey City, NJ, USA

Mild to moderate Alzheimer’s disease (AD) is currently treated with cholinesterase inhibitors (ChEIs), while moderate to severe AD is treated with the N-methyl-D-aspartate (NMDA) receptor antagonist memantine and the cholinesterase inhibitor donepezil. The purpose of this study is to review the safety and tolerability data for ChEIs and memantine, based upon manufacturers’ data found in the prescribing information. Prescribing information was obtained from the package inserts of memantine, donepezil, rivastigmine, and galantamine. The safety information from each prescribing information document was extracted and analyzed for trends in safety and tolerability for each medication, compared to placebo. An inspection of prescribing information data indicated that the ChEIs donepezil, rivastigmine, and galantamine are associated with cholinomimetic effects. Nausea and vomiting were consistently reported across all ChEI trials as the most common reasons for trial discontinuation. Dizziness, anorexia, and diarrhoea were also commonly reported adverse events (AEs) in all ChEI trials. The most frequently reported AEs in memantine trials were dizziness, headache, and confusion. No AEs led to trial discontinuation in >1% of patients at a frequency greater than placebo. From a regulatory point of view, all currently marketed AD treatments are safe and tolerable, including the co-administration of an NMDA receptor antagonist and a ChEI. Although it is difficult to make comparisons between drugs studied in different trials, available data suggest that AEs most commonly observed in the ChEIs trials (gastrointestinal AEs) are typical of that drug class. Memantine provides an alternative or concomitant therapeutic option with a distinct AE profile.

**P2091**  
**DOES THE COGNITIVE PROFILE SCATTER IN EARLY DETECTION OF COGNITIVE DECLINE?**

N. Attia Romdhane 1, T. Bellaj 2, A. Mrabet 1  
1Department of Neurology, Charles Nicolle Hospital, 2Department of Psychology, Human and Social Sciences Faculty, Tunis, Tunisia

**Background and aims:** Many authors agree that future treatments should focus on the earliest stages of cognitive decline according to aetiology. We think that cognitive profile scatters are more accurate than global tests scores for early detection of cognitive decline.

**Method:** A cross sectional case control study includes 176 subjects classified, according to latest consensus, as normal, MCI or demented after a complete neurological exam, neuroimaging, biology, and neuropsychological testing (golden standard). MMSE, ADAS-Cog and T-MMS90 are evaluated with cut-offs according to age and education. T-MMS90 includes items assessing attention, short term, working, episodic and semantic memories, executive functions, language, praxis and orientation. For scatters, each T-MMS90 subtest score is standardized according to age and education.

**Results:** To detect MCI and dementia cases, tests scores show weak Youden indexes (MMSE=0.21, ADAS-Cog=0.42, T-MMS90=0.42). T-MMS90 scatters are very sensitive (94%) and allow detection of MCI or dementia type. In Amnestic MCI, episodic memory is abnormal (recall and recognition ≤ 2 STD). Non Amnestic MCI (normal episodic memory), is of Frontal subtype if executive functions are ≤ 2 STD and of Levy Body subtype if attention and short term memory are ≤ 2 STD. At dementia stage, major functions are more impaired (≤ 3 STD) while at least one new function is abnormal (≤ 2 STD).

**Conclusions:** Global tests scores are not reliable for early detection of cognitive decline. T-MMS90 scatters are very sensitive and allow detection of MCI or dementia type. Exploiting scatters should improve clinical trials enrolment and evaluation criteria.
P2092

A CASE OF POSTERIOR CORTICAL ATROPHY
J.S. Baik, J.H. Park, J.Y. Kim, S.W. Han
Department of Neurology, Inje University, Sanggye Paik Hospital, Seoul, South Korea

Background: Posterior cortical atrophy is a subgroup of focal cortical atrophy with progressive degenerative dementia that begins with higher visual dysfunction.

Case: A 51-year-old man presented with visual disturbance for several months. He was a taxi driver and when he came to the hospital, he could not drive a taxi because of geographical disorientation, impairment of calculation and writing. So he experienced car accidents frequently. On examination, he had a Balint syndrome, visuospatial dysfunction, prosopagnosia, apraxia and Gerstman syndrome. Brain MRI showed marked atrophy especially in both occipito-parietal areas, more pronounced on the left. SPECT with HMPAO disclosed hypometabolism on bilateral occipito-parietal area, more marked on the left rather than right.

Conclusion: We present a patient who was diagnosed as posterior cortical atrophy. Some evidences on imaging and clinical features are consistent with posterior cortical atrophy which is variants of Alzheimer’s disease.

P2093

DISSEMINATED VARICELLA ZOSTER IN A 92-YEAR-OLD
R. Bhatnagar, T. Solanki
Care of the Elderly Department, Taunton and Somerset NHS Trust, Taunton, Somerset, UK

We describe an unusual case of Varicella zoster virus (VZV) in an otherwise well 92-year-old. Presentation was following a fall and confusion, which had happened within two days. She had a Glasgow coma scale score of 11 and was confused. She had generally increased tone. There was a coalescing vesicular rash on the left side of her chest in a T6-8 dermatomal distribution. There were further vesicles on the trunk which were spreading. An initial diagnosis of ‘shingles’ with confusion of unclear cause was made. She was dehydrated as she had been vomiting and there was slight hypotension. Lumbar puncture revealed a lymphocytosis with mildly elevated protein and low glucose. Based on this, she was treated with antiviral and broad-spectrum antibiotic medication. They were modified to intravenous acyclovir only following confirmation of positive PCR test for varicella zoster virus from the CSF. The rash improved and wakefulness returned over the following 2 weeks. The patient remained dependent and confused, having previously been living alone independently.

VZV is a common pathogen, but in this case presented in its rare disseminated form, with meningencephalitis and widespread cutaneous involvement. Disseminated VZV has been previously described but usually occurs in patients known to be immunocompromised. Our case demonstrates that supposedly healthy patients, especially the elderly, are at risk of this condition and it should be considered as a diagnosis in the presence of a rash and confusion.

P2094

DEMENTIA DIAGNOSTIC ACCURACY OF FOTOTEST IN FOTOTRANS STUDY
C. Carnermo-Pardo1, A. Zambrano Toribio2, R.J. de la Vega2, N. Rodriguez Espinosa2, M. Baquero Toledo2, S. Coudisi Martinez-Conde1, A. Ortega Morenol1, R. Vilchez Carrillo1, on behalf of FOTOTRANS Study Group
1Hospital Universitario Virgen de las Nieves, Granada, 2Hospital Punta de Europa, Algeciras, Cadiz, 3Hospital Universitario San Cecilio, Granada, 4Hospital Universitario Centres de Asturias, Oviedo, 5Hospital Sant Camil, Sant Perer de Ribes, Barcelona, 6Hospital de Navarra, Pamplona, Spain

Introduction: The Fototest (www.fototest.es) is a simple short (<3-min) test applicable to illiterate subjects and its results are not influenced by age or educational level. FOTOTRANS is a cross-sectional multi-centre study with the objective of evaluating the DA of the Fototest under routine clinical conditions.

Methods: The Fototest, Eurotest and verbal fluency test (VFT) were applied to neurological patients aged >60 years; the Mini-Mental test (MMSE) was also applied to a sub-sample. Patients were classified as “Non-Demented” (ND) or “Demented” (DEM) [DSM-IV criteria]. We calculated sensitivity (Sn) and specificity (Sp) values with their corresponding 95% interval and the area under the ROC curve (AUC), which was used to compare the DA of the different instruments.

Results: 20 neurologists selected a total of 627 subjects: 467 ND, 122 DEM and 38 excluded patients (due to incomplete data or protocol violations). The best cut-off Fototest score was 26/27, with a Sn of 0.88 (0.81–0.94) and Sp of 0.87 (0.84–0.90). Both Fototest and Eurotest showed a high DA (0.94±0.01, AUC±SEM) that was superior to that of VFT (0.90±0.01) and MMSE (0.91±0.03), although the difference was only significant with respect to that of the VFT (p<0.01).

Conclusions: In this large and naturalistic sample of neurological patients with very low educational level, the Fototest showed a high diagnostic accuracy for dementia, similar to that of the Eurotest and MMSE, despite being much easier to apply and taking less than three minutes.

Partially supported by JANSSEN CILAG SA and Junta de Andalucia (Exp. 441/06) grants.
tocol violations). The DA of the Fototest (0.86±0.01, AUC±SEM) was superior to that of the Eurotest (0.84±0.01), VFT (0.78±0.02) and MMSE (0.83±0.04), although the difference was only significant with respect to that of the VFT (p<0.001).

**Conclusions:** All screening tests showed only a modest DA (<0.90), therefore a strategy of dichotomized results (positive/negative) cannot be effective for the detection of CI with these instruments. The Fototest has the advantages of simplicity, speed and the non-influence of educational factors.

Partially supported by Junta de Andalucía (Exp. 441/06) grants.

---

**P2096**

**CHARACTERISTICS OF COGNITIVE IMPAIRMENT IN SUBCORTICAL VASCULAR DEMENTIA**

R. Chirileanu1,2, M. Simu1,2, D. Reisz1,2, R. Popa1,2, C. Socoliu1,3,4

1University of Medicine and Pharmacy Timisoara, 2Neurology Clinic, 3Emergency Clinic, 4Neuroimagistic Department, Hospital Timisoara, Romania

**Background and aim:** Causes of cognitive impairment in subcortical cerebrovascular disease are related to the damage of the frontostriatal loops that determine frontal lobe dysfunction. This means the predominant impairment is associated with the executive function and affects secondarily associated cognitive functions such as memory. The aim of the study is to evaluate the characteristics of the cognitive decline, the neuropsychological profile related to the subcortical lacunar infarcts evidenced on the MRI.

**Methods:** The subjects of this study were 50 patients diagnosed with Mild Subcortical Vascular Dementia according to the NINDS AIREN criteria, compared to 49 controls with subcortical cerebrovascular disease, lacunar infarcts, without dementia. All subjects underwent MRI examination –measurements of volume of lacunar infarcts in subcortical structures, volume of white matter lesion, cortical atrophy- volume of gray matter, hippocampal volume. The neuropsychological evaluation consisted of tests of global cognitive function, memory, language and executive function.

**Results:** In vascular dementia patients 90% had problems in writing a sentence, 63% had problems in remembering, 32% had problems in drawing, 51% had problems in calculating. The cognitive effects of the small vessel cerebrovascular disease are variable and not especially distinct.

**Conclusions:** The neuropsychological tests showed that mild demented patients had predominant executive dysfunctions and not memory complaints. Cognitive impairment seems to be related to hippocampal changes and cortical atrophy.

---

**P2097**

**ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM PRESENTING WITH DEMENTIA**

S.G. Papageorgiou, Y. Christou, T. Kontaxis, A. Bonakis, C. Potagas, M. Anagnostouli, N. Kalfakis

Neurology Department, Eginition Hospital, Medical School, University of Athens, Greece

**Introduction:** Primary Hyperparathyroidism (PHPT) involves primarily the kidneys, the skeletal system, the gastrointestinal tract and rarely the nervous system and muscles. We present an exceptional case of asymptomatic primary hyperparathyroidism presenting with dementia.

**Case-report:** A 76-year-old female patient presented with a 2-year history of progressive memory impairment, cognitive deficit (especially concentration and attention), apathy and gait impairment. One year before she was diagnosed with Alzheimer’s disease; she started treatment with donepezil for one year with no significant improvement. An extensive blood and biochemical control revealed a high serum Calcium (11.7 mg/dl) and high (77.5) PTH. Ultrasound of thyroid and parathyroid glands revealed an adenoma of right parathyroid gland and a nodular morphology of thyroid gland with normal thyroid hormones and anti-thyroid Ab. Detailed investigation for causes of secondary hyperparathyroidism was negative. Due to absence of symptoms of hyperparathyroidism and severe hypercalcemia, she was initially treated conservatively. At referral time, the neurological picture consisted of: mild extra-pyramidal signs, moderate dementia (MMSE=15) and severe behavioural disturbances. Because of the continuous aggravation of the cognitive deficit, parathyroidectomy was performed. 3 weeks after the surgery, the neurological picture dramatically improved. Parkinsonism and behavioural disorders were remarkably reduced and MMSE score raised to 25.

**Discussion:** Cognitive and behavioural disorders can exist in PHPT. However, PHPT presenting only with dementia is exceptional. The significant improvement in the case of our patient suggests that parathyroidectomy should be considered in patients with severe CNS complications, even in the absence of other symptoms of hyperparathyroidism.

---

**P2098**

**BEHAVIOURAL EFFECTS OF MEMANTINE: UNDERSTANDING THE PHARMACOLOGICAL RATIONALE**

P.T. Francis

Wolfson Centre for Age-Related Diseases, King’s College London, UK

Behavioural symptoms are a significant problem in Alzheimer’s disease (AD). Symptoms such as agitation/aggression and psychosis reduce patient quality of life, significantly increase the burden on caregivers, and often trigger nursing home placement. However, existing behavioural treatments have been associated with safety concerns, and the FDA has issued warnings for the use of atypical antipsychotics in dementia patients, due to increased mortality risk. The NMDA receptor antagonist – memantine – is indicated for the treatment of moderate to severe AD, and has been shown to improve behavioural aspects of AD, including agitation/aggression, and delusions. Furthermore, memantine has a beneficial effect on cognition and function in AD, and displays a favourable tolerability profile. Therefore, it is relevant to investigate the underlying mechanism linking memantine with the behavioural elements of AD. Frontal and cingulate cortices are proposed as regional substrates of agitation and aggression. One hypothesis proposes that memantine corrects dysfunctional glutamatergic neurotransmission in the frontal and cingulate cortices, thereby normalising pathways responsible for causing agitation. To this end, glutamatergic dysfunction occurs in many cortical regions of patients with AD, perhaps triggered by the glutamate elevation induced by beta-amyloid. However, to date, no study has examined this in relation to agitation/aggression. Agitation/aggression may be linked to the abundance of hyperphosphorylated tau protein in the frontal cortex. Memantine has been shown to reduce tau phosphorylation via GSK-3b (kinase) or activation of PP2A, which might subsequently lead to reduced agitation. Further investigation into the action of memantine may help explain the process underlying behavioural symptoms in AD.
P2099
EFFECTS OF GALANTAMINE IN PATIENTS WITH ALZHEIMER’S DISEASE (AD) PREVIOUSLY TREATED WITH ANTIDEMENTIVE DRUGS IN GERMANY – A NON-INTERVENTIONAL STUDY (GAL-DEM-4005)
B. Ibach, M. Gervc, J. Czekalla
Therapeutic Area CNS, Department of Medical and Scientific Affairs, Janssen-Cilag GmbH, Neuss, Germany

Background: Lack of individual response to antidementive drugs or AEs may require alternative treatment strategies in AD. This non-interventional trial assessed the effectiveness and tolerability of galantamine in patients who had been transitioned from therapies currently used in Germany.

Methods: In this prospective, non-interventional trial, patients with mild to moderate AD (ICD-10) were treated with 8-24 mg/d galantamine and observed for 6 months. Clinical assessments included DemTect, NOSGER, Zarit Burden Interview (ZBI) and CGI. Statistical analyses based on intent-to-treat population (LOCF; t-test and Wilcoxon-test for dependent samples).

Results: 279 patients (48% mild, 52% moderate AD; mean age±SD 75.4±8 years; 54.5% women) were enrolled. 77.3% completed the study. 10.1% discontinued due to AEs. After 159±50 days of treatment mean total DemTec-t-scores changed from 7.2±3.5 to 8.2±4.4 (p<0.0001). 82.6% of patients with nootropic, 72.1% with other AChEI, 70% with memantine pre-treatment experienced clinical response (defined as change of DemTect raw values up to a decline of ≤2 pts). NOSGER scores did not change, with exception of enhanced mood (p=0.05). ZBI remained stable. CGI demonstrated improvement or stabilization for 75.5% of patients. 35.0% had at least one AE. Most frequent AEs (>5%) were nausea, agitation and dizziness. 23 patients experienced a SAE with 2 considered possibly related to galantamine (syncope, fall). 1 death (fall with traumatic brain injury) was rated as possibly related to galantamine.

Conclusions: This non-interventional trial supports galantamine to be efficacious and well tolerated in patients with mild to moderate AD previously treated with nootropics or other antidementive drugs.

P2100
DEFICIENCY OF FOLIC ACID AND VITAMIN B12, DYSLIPIDEMIA, HYPERHOMOCYSTEINEMIA IN DIFFERENT TYPES OF VASCULAR DEMENTIA
A. Graban1, M. Bednarska-Makaruk1, A. Bochynska1, W. Lipczynska-Lojkowska1, H. Wehr1, D. Ryllewicz1
11st Neurology Department, 2Department of Genetics, Institute of Psychiatry and Neurology, Warsaw, Poland

Disturbances of homocysteine (Hcy) metabolism favour atherosclerosis development in both small and large brain vessels. This increases the risk of incidents of vascular origin like subcortical lacunar strokes (S-VaD) or multifarctus in strategic areas (M-VaD). The aim of this study was to estimate the levels of Hcy, folic acid, vitamin B12 and lipids in both forms of dementia of vascular origin (VaD).

Material: The patients were divided into two subgroups: 60 patients with S-VaD and 34 with M-VaD. The control group consisted of 126 persons without dementia.

Diagnosis was based on DSM-IV, NINCDS and AIREN criteria and ischemic Hachinsky scale.

Methods: Homocysteine was determined by ELISA method using Boehringer kits. Folic acid and vitamin B12 were estimated by chemiluminescent methods and lipids by enzymatic methods.

Results:
1. Hyperhomocysteinemia was significantly more frequent in VaD patients than compared to controls. No group significant differences were stated between subcortical and multifarct dementia.
2. Folic acid and vitamin B12 deficiencies were observed more frequently (close to significant) only in individuals with M-VaD.
3. In M-VaD individuals low HDL (high density lipoprotein) cholesterol was observed more frequently than in the controls.

Conclusion: Hyperhomocysteinemia is a common symptom in dementia of vascular origin.

P2101
APOLIPOPROTEIN E PHENOTYPE & DEMENTIA IN GREEK PATIENTS WITH EXTRAPYRAMIDAL SYNDROME
E. Hatzifilippou1, M. Arnaoutoglou1,2, E. Koutsouraki1,2, C. Karamanidis1, M. Traka1, T. Banaki1, V.G. Costa1,2, S.J. Baloyannis1,2
11st Department of Neurology, 2Neuropatological Laboratory of the 1st Department of Neurology, Aristotelian University, AHEPA Hospital, Thessaloniki, Greece

Apolipoprotein E gene (APOE) polymorphism is an important determinant for the development of various cardiovascular and neurodegenerative disorders. The apolipoprotein E (ApoE) ε4 allele has been associated with an increased risk of A.D. Although this allele has been linked to earlier onset of Parkinson’s disease, a correlation with dementia in PD has been only inconsistently demonstrated. The aim of our investigation was to associate the ApoE polymorphism with dementia in Greek patients suffering from extrapyramidal syndrome. We have examined 11 patients (8 females and 3 males) with a male to female ratio of 1:2.6 at a mean age of 62 years old. Genomic DNA was isolated from whole blood by the use of the commercial available WIZARD® Genomic DNA Purification kit. For the amplification of the fourth exon from ApoE gene locus as well as for the genotyping of Apo E2, E3, E4 we used the commercial available INNO-LiP ApoE kits. 82% of the patients revealed the E3/3 phenotype but only 18% of them demonstrated the E3/2. Our present results indicate that the most common ApoE genotype in Greek patients suffering from extrapyramidal syndrome, is the E3/3. According to our investigation there was no association between the ε4 allele and the disease. We also confirm the absence of correlation between the grade of dementia and ApoE phenotypes. Further investigation should be done.

P2102
LATE-ONSET AUTOSOMAL DOMINANT ALZHEIMER’S DISEASE
P. Hancock1, A.J. Larner1
1The Brooker Centre, Rancon, 2Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Objective: To report a family with late-onset Alzheimer’s disease (AD) fulfilling criteria for autosomal dominant transmission.

Methods and setting: Psychiatric ward; Cognitive Function Clinic.

Results: Proband was a 78-year-old man with a 6-month history of progressive memory impairment, complicated by behavioural and psychiatric symptoms, who fulfilled NINCDS-ADRDA clinical diagnostic criteria for probable late-onset AD. CT brain scan showed generalized cortical atrophy. Family history revealed 6 additional cases of AD in 2 generations, fulfilling strict criteria for autosomal dominant transmission (23 affected family members in at least 2 generations). As far as it could be ascertained, all had age of onset >65 years. Neurogenetic testing of the proband for mutations
in the presenilin-1 gene, which have on occasion been associated with late-onset autosomal dominant AD, was negative.

**Discussion and conclusions:** Pedigrees with late-onset autosomal dominant AD may be informative in the search for novel genes indicating AD.

**P2103**

**CHOLESTEROL LEVEL IN ALZHEIMER’S DEMENTIA**

Z. Trkanjec, V. Basic Kes, I. Martinic Popovic, M.J. Jurasic, V. Seric, M. Lisak, V. Demarin

*Department of Neurology, Sestre Milosrdnice University Hospital, Zagreb, Croatia*

The aim of study was to evaluate the levels of cholesterol in patients with Alzheimer’s dementia (AD) and vascular dementia (VaD). 66 patients with dementia were enrolled in this study. AD was diagnosed in 43 and VaD in 23 patients. In a group of 43 patients (22 males and 21 females) with AD, mean age 72.79 years (standard deviation /SD/=8.19 years), and in a group of 23 patients with VaD, mean age 77.43 (SD=7.58) plasma values of cholesterol were analyzed. In AD group 18 patients had normal, while 25 had elevated plasma cholesterol levels, while in VaD group 12 patients had elevated and 11 had normal plasma cholesterol levels. Mean plasma level of total cholesterol was 5.39 (SD=1.05), LDL cholesterol was 3.33 (SD=0.95), and HDL cholesterol was 1.41 (SD=0.34) in patients with AD. In patients with VaD mean plasma level of total cholesterol was 5.78 (SD=1.06), LDL cholesterol was 3.72 (SD=0.85) and HDL cholesterol was 1.44 (SD=0.57). The levels of cholesterol, LDL cholesterol, HDL cholesterol were higher in the group of patients with VaD, but the difference did not receive statistical significance. Our data show that patients with AD have elevated plasma levels of cholesterol. Results of this study support the idea that cholesterol could have some influence on etiology, onset and progression of AD, as well as on pathogenesis of VaD.

**P2104**

**ACCEPTANCE OF MEMORY-AMBULANCES**

W.D. Moller1, S. Sprenger1, P. Kropp1

1Creutzfeld Institute, Kiel; 1Institute of Medical Psychology, University of Rostock, Germany

**Introduction:** Today memory ambulances are part of neurological or psychiatric clinics. Aim of the present study is to count visits for memory ambulances compared with visits 15 years ago.

**Methods:** We compared the number of patients in 1991 and 1992 with 2002 to 2006. All patients who visited our memory-ambulance for the first time were evaluated by Mini-Mental-State-Examination (MMSE, Folstein 1990) and scored into mild, moderate, or severe dementia of Alzheimer’s type (DAT), vascular dementia (VD), or other (e.g. depression).

**Results:** Between 1991 and 2006 yearly 650 patients visited our ambulance. In 1991 and 1992 yearly 13 patients (2%) suffered from dementia (2 mild, 7 moderate, 4 severe, 50% DAT, 40% VD). In the last years more than 30 demented patients (4.6%) were diagnosed each year (10 mild, 14 moderate, 6 severe, 45% DAT, 45% VD).

**Discussion:** Compared with former years, nowadays more patients with cognitive problems come to the specialist. Because the intensity of dementia is lower now than 15 years ago, we conclude that patients come earlier to the ambulance. This could be the positive effect of self-help support groups and a pronounced awareness within the population.

**P2105**

**MIGRAINE AND DEMENTIA**

W.D. Moller1, P. Hossfeld1, P. Kropp1

1Creutzfeld Institute, 1Institute of Sports, University of Kiel, 1Institute of Medical Psychology, University of Rostock, Germany

**Introduction:** There are only few studies which observe simultaneous migraine and dementia of Alzheimer’s type (DAT) in elderly patients. Aim of the present study is to observe incidence of migraine in a sample of patients with DAT and vascular dementia (VD).

**Methods:** A sample of 94 DAT patients and 40 patients suffering from VD were examined. Additionally data from patients’ relatives were collected to estimate migraine lifetime-prevalence according to the revised IHS criteria. Dementia was mild or moderate according to the Mini-Mental-State-Examination (Folstein 1990).

**Results:** In one DAT-patient (1%), but in 3 VD-patients (7.5%) migraine according to the IHS criteria could be diagnosed.

**Discussion:** Incidence of migraine in VD patients follows those of the general population, but not so in DAT. It should be discussed whether migraine and DAT may be incompatible diseases. Obviously patients with VD own a vascular system which is similar or corresponding to that of patients with migraine.

**P2106**

**MORPHOLOGICAL AND MORPHOMETRIC STUDY OF CA3 NEURONAL EXCRESCENCES IN THE HUMAN HIPPOCAMPUS IN NORMAL CONTROL AND ALZHEIMER’S DISEASE PATIENTS**

K. Tsamis1, D. Mytilinaios1, J. Mavroudis1, S.N. Njau1, D. Psaroulis2, V. Kosta2, S.J. Baloyannis1

1Laboratory of Neuropathology, 1st Department of Neurology, 2Institute of Medical Psychology, Aristotle University of Thessaloniki, Greece

The pyramidal neurons of the CA3 area of human hippocampus as well as the hilar mossy neurons possess large and branched dendritic spines, named “excrescences”. These dendritic structures were studied and compared in CA3 area of hippocampus in two patients suffering from Alzheimer’s disease, 4 age-matched controls and 3 younger controls. In order to perform our study, we applied the silver Golgi impregnation technique, which allows the visualization and description of the morphologic characteristics of the excrescences (especially in the apical dendrite) under light microscopy. Furthermore, we performed a morphometric analysis of the density and the average height of the excrescences on the apical dendrite. This analysis revealed reduced density and increased height in Alzheimer’s disease patients despite a fluctuation of the results.

**P2107**

**NEUROPHYSIOLOGIC AND CLINICAL SIGNS OF MOTONEURONAL DEGENERATION IN FRONTO-TEMPORAL DEMENTIA**

V. Navarra, V. La Bella, C. Cupidi, P. Mattaliano, F Piccoli, T. Piccoli

Neuroscienze Cliniche, Neurologia E Psichiatria, Policlinico, Palermo, Italy

**Background and Aim:** It has been suggested that frontotemporal dementia (FTD) and motoneuron disease (MND) represent a continuum in a clinicopathological spectrum. Differently from cognitive impairment in MND, motoneuron involvement was poorly investigated in FTD. This study was aimed to identify clinical and neurophysiologic signs of MND in patients with FTD, without a previous diagnosis of MND.
Materials: A clinical and EMG examination were performed on 10 patients with FTD, diagnosed according to Neary criteria, to evaluate the presence of upper (UMN) and lower motoneuron (LMN) signs, as listed in revised El Escorial criteria for ALS. Brainstem, cervical, thoracic and lumbar regions were explored. The patients had no known diagnosis of MND and were not selected on the presence of motor signs.

Results: 9 out of the 10 patients showed clinical motoneuronal signs, involving both UMN and LMN in 6 patients and UMN alone in 3 patients. An EMG study revealed active and chronic denervation in 9 patients. Clinical and EMG signs always affected 2 different regions at least for both UMN and LMN in all patients except one. Brainstem, cervical and lumbar regions were equally impaired among the patients.

Conclusions: 9 of the 10 patients with FTD showed evidence of MND, suggesting a frequent overlap between these entities. Neurophysiologic examination improved detection of LMN signs. A preferred site of impairment was not observed between explored regions. Follow-up study is in progress to verify the progression of MND in these patients.

P2108
AN INTERESTING CASE OF PRIMARY PROGRESSIVE APHASIA (PPA)
J. Njeukui Tchoua, P. Seeldrayers, J. Jacquy
Department of Neurology, CHU Charleroi, Charleroi, Belgium

Primary progressive aphasia (PPA), initially defined by Mesulam, is a clinical syndrome characterized by the insidious occurrence and progressive worsening of a language disorder without involvement of other cognitive functions at least the first two years of the disease. The PPA is generally classified in non fluent and fluent. Clinical Case: M.D., a right handed 84-year-old male, former engineer, presented for several months difficulties of speech. He is a fan of cross word puzzles, figures and letters; now he has difficulties to devote himself to his hobby. He consulted us the first time in 2005. The CT scan was normal. The spect shows a hypoactivity of the fronto-temporal zones bilateral. The EEG is slow. With the MMS, one notes small language difficulties in the answers of the fronto-temporal zones bilateral. The EEG is characterized by a dysorthography. The tests of visual gnosy and colour are carried out in a correct way.

Conclusion: The progressive course of the disease was present in 15 patients (28.3%) from the group I in comparison with 12 patients (22.6%) from the group II. Chi2=0.44, p>0.05

P2110
HIGH SERUM CHOLESTEROL LEVEL AND MCI COURSE
A. Pfeffer1, M. Chodakowska-Żebrowska1, A. Barczak1, E. Łuczywek2, B. Wasiaκ1, M. Barcikowska1
1Department of Neurodegenerative Disorders, Medical Research Centre, Polish Academy of Sciences, 2Neurological Department, CSKMSWiA, Warsaw, Poland

Background: A large number of variables appeared to be predictors of dementia in subjects with mild cognitive impairment (MCI). Some epidemiological studies suggest the link between the cholesterol level and the development of Alzheimer’s disease. However, prognostic significance of high serum cholesterol level in MCI patients remains unclear.

Objective: To test the hypothesis that high total cholesterol level in MCI patients increase the risk of progressive course of the disease.

Material and methods: The subjects of this study were 106 patients with MCI, diagnosed according to the criteria proposed by Petersen et al. (1997). All subjects were given blood samples for serum cholesterol level at the initial visit. The mean follow-up period for the cohort was 2.2 years. At follow-up, all patients were divided into 2 groups: I: 53 subjects with normal cholesterol level, II: 53 subjects with raised cholesterol level (>200 mg/dl). The number of patients with progressive symptoms of cognitive impairment or conversion to dementia was compared in both groups.

Results: The progressive course of the disease was present in 15 patients (28.3%) from the group I in comparison with 12 patients (22.6%) from the group II. Chi2=0.44, p>0.05
Conclusion: High total cholesterol level is not associated with increased risk of progressing course of cognitive impairment and dementia in our group of MCI patients.

**P2111**

**FRONTAL BEHAVIORAL INVENTORY (FBI) IN AN OUTPATIENT MEMORY CLINIC IN GREECE**


**Neurology Department, General Hospital of Athens, Greece**

**Aim:** To study a Greek translation of FBI.

**Methods:** The 350 caregivers have answered the questionnaire.

**Results:** There is a significant difference between the FBI-total score of the frontal-behavioral-variant FTD and other types of dementia. There is no difference between the fbvFTD and the other types of the FTD-spectrum.

**Conclusions:**
1) The FBI can dx fbvFTD
2) It can not discriminate among the different types of FTD (advanced stage of those patients).

<table>
<thead>
<tr>
<th>MED DIAGNOSIS</th>
<th>No</th>
<th>MMSE</th>
<th>FBI Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>21</td>
<td>29.9</td>
<td>5.52</td>
</tr>
<tr>
<td>MCI (Mild Cognitive Impairment)</td>
<td>106</td>
<td>27.2</td>
<td>10.7</td>
</tr>
<tr>
<td>AD (Alzheimer’s disease)</td>
<td>80</td>
<td>16.5</td>
<td>21.5</td>
</tr>
<tr>
<td>AD+CVD (Cerebrovascular dis.)</td>
<td>37</td>
<td>19.5</td>
<td>23.4</td>
</tr>
<tr>
<td>LBD (Lewy body dementia)</td>
<td>17</td>
<td>20.0</td>
<td>22.5</td>
</tr>
<tr>
<td>VAD (Vascular dementia)</td>
<td>13</td>
<td>22.3</td>
<td>21</td>
</tr>
<tr>
<td>PD (Parkinson’s dis.)</td>
<td>7</td>
<td>26.2</td>
<td>17.8</td>
</tr>
<tr>
<td>DPR (Depression)</td>
<td>17</td>
<td>28.7</td>
<td>10.4</td>
</tr>
<tr>
<td>FTD (fbvFTD)</td>
<td>24</td>
<td>14.2</td>
<td>35.6</td>
</tr>
<tr>
<td>Other types of the FTD spectrum and related disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPA (Primary non-fluent aphas</td>
<td>6</td>
<td>12.1</td>
<td>33.3</td>
</tr>
<tr>
<td>SD (Semantic dementia)</td>
<td>15</td>
<td>12.5</td>
<td>33.5</td>
</tr>
<tr>
<td>MND (Motor neuron dis.)</td>
<td>3</td>
<td>22.6</td>
<td>22.6</td>
</tr>
<tr>
<td>CBD (Corticobasal degeneration)</td>
<td>4</td>
<td>19.0</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>350</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**P2112**

**A RARE CASE OF FRONTOTEMPORAL DEMENTIA AND MOTOR NEURON DISEASE: A CLINICAL, NEUROPSYCHOLOGICAL AND RADIOLOGICAL INTER-RELATION**

H. Sarac1, D. Vranjes2, M. Zagar2, N. Henigsberg1, E. Bilic2, I. Kostovic1

1Diagnostic Centre, 2University Department of Neurology, Zagreb School of Medicine and University Hospital Centre, Zagreb, Croatia

**Background:** Motor neuron disease (MND), rarely (3–5%) arises with frontotemporal dementia (FTD). The frequency of MND/FTD in Croatia is unknown (but extremely rare). Magnetic resonance spectroscopy (MRS) has been introduced as a biomarker in detection and quantification of neurodegenerative changes in MND and FTD solely, but a few and far between findings on MRS in MND/FTD syndrome show that these data are insufficient.

**Case Description:** A 54-year-old female exhibited upper limb weakness, dysarthria, dysinhibition and a deficit in cognitive functioning presented. EMG detected severe lower motor neuron loss. Lund and Manchester mental status and consensus criteria indicated FTD. MRI demonstrated cortical atrophy in frontal and temporal lobes, hypointensity in the motor cortex and hyperintense corticospinal tract. Spectroscopic MR demonstrated severe and specific reduction in NAA/Cho, inverted glutamate peak and increased Cho/Cr highly likely to MND.

**Conclusion:** Clinical diagnostic sensitivity in MND/FTD could be improved by neuropsychological and radiological techniques where MRS may quantify neurodegenerative changes. We observed that severe reduction in NAA/Cho, glutamate and elevated Cho/ml may be detected in the MND/FTD, which is unlikely to FTD. We and others suggest that MND, MND/FTD and FTD represent a clinical range of a pathological continuum. Referring to this case and a few previous cases, MRS could be used in early detection and follow-up studies as a meaningful biomarker in MND/FTD syndrome.

**P2113**

**AN UNUSUAL CAUSE OF FALLS IN THE ELDERLY**

C. Chamberlain, T. Solanki

Care of the Elderly Department, Taunton and Somerset NHS Trust, Taunton, Somerset, UK

**Case study:** A 90-year-old person presented with multiple falls. No precipitating features of the collapse episodes were found in her history. Her past medical history included a previous cervical decompresion for a pseudotumor using an anterior approach. Examination demonstrated increased upper limb tone and more brisk upper limb than lower limb reflexes and inverted supinator jerks. MRI revealed impingement of the upper cervical cord and subluxation of C1 on C2. The subluxation was attributed to her previous surgery resulting in damage to the transverse ligament of atlas.

**Literature review:** A literature review was undertaken through the Cochrane database, Medline and Google. Unpublished articles or non-English speaking language articles were not included

**Results:** The published literature is limited, and focuses on case studies. No formal meta-analyses were available. The results suggest that spinal compression is a rare, but significant cause of falls in the elderly. In light of the paucity of the evidence base, it is possible that cervical spine disease is not considered as a cause of recurrent falls.

**Conclusions:** Spinal compression is a potentially reversible cause, which, if recognised and treated, patients could profit substantially. We suggest that cervical spine disease should be considered as a potentially reversible cause of falls among recurrent fallers in whom other investigations are negative

**P2114**

**GALANTAMINE EXTENDED-RELEASE IN ALZHEIMER’S DISEASE (AD): DEMENTIA SEVERITY CUT-POINTS BASED ON UK NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE (NICE) CRITERIA AND COMMONLY USED DEFINITIONS**

K. Sorr1, Y. Zhu2, S. Schwalen3, J. Amatniek1

1Arroscience Inc., Toronto, ON, Canada, 2Ortho-McNeil Janssen Scientific Affairs LLC, Titusville, NJ, USA, 3Janssen-Cilag GmbH, Neuss, Germany

**Aim:** To assess safety and efficacy of galantamine extended-release (GAL-ER) in mild or moderate AD patients based on NICE criteria (MMSE ≥ 20 for mild AD; MMSE 10–20 for moderate AD) relative to common MMSE cut-points used clinically (MMSE ≥18 for mild; MMSE <18 for moderate AD).

**Methods:** GAL-ER (n=319) and placebo-treated subjects (n=320) with baseline MMSE 10–24 were included in this post hoc analysis of a 6-month randomized, double-blind trial (Brodaty et al. Dement Geriatr Cogn Disord 2005; 20:120–132). Subjects were stratified according to mild or moderate disease severity at baseline. Mean change in ADAS-Cog 11 was evaluated, and descriptive methods were used for adverse event reporting.

**Results:** For moderate AD, mean changes in ADAS-Cog 11 from baseline were -2.4 points (mean change, -0.66 vs. +1.77 [p<0.0001]) and -2.5 points (mean change, -0.46 vs. +2.08 [p<0.0007]) for GAL-ER versus placebo, based on NICE and commonly used
clinical cut-points, respectively. For mild AD, mean changes in ADAS-Cog 11 scores from baseline were –2.2 points (mean change, –2.31 vs. –0.13 points \([P=0.0021]\)) and –2.3 points (–1.83 vs. +0.43 \([P=0.0001]\)) for GAL-ER versus placebo, based on NICE criteria and commonly used clinical cut-points, respectively. Adverse events reported by 25% of subjects, and at a rate of at least twice of that for placebo, were nausea, vomiting, and anorexia in the NICE-defined moderate group, and nausea, dizziness, vomiting, anorexia, fatigue, depression, and weight decrease in the mild group. **Conclusion:** GAL-ER treatment resulted in cognitive improvement, regardless of mild or moderate disease severity at baseline.

**P2115**

**PSYCHIATRIC ONSET IN FAMILIAL CREUTZFELDT JAKOB DISEASE**

M. Valentí Soler¹, E. García Fernandez², J. Arpa Gutierrez², C. Morales Bastos³, M. Gutierrez Molina³, F. Vivancos Matellano⁴, F. Grau⁵

¹Department of Neurology, ²Unit of Neuropathology, La Paz University Hospital, Madrid, ³Department of Neurology, Clinic University Hospital, Barcelona, Spain

**Objective:** To describe the unique case of familial Creutzfeldt Jakob disease (CJD) with psychiatric symptoms at onset in our hospital. Psychiatric onset only appears in 6% of CDJ cases. Familial cases are less than 5% of CJD patients in Spain. Clinico-pathologic case: A 58-year-old woman was admitted to psychiatry with a one-year history of progressive anxiety, emotional liability, attention deficit, memory impairment and suicidal ideation. During follow-up in the Department of Psychiatry, global aphasia and cerebellum ataxia became evident within 9 days. In the Department of Neurology she developed withdrawal, dementia, pyramidal and extrapyramidal signs, myoclonus, akinetic mutism and seizures in a rapidly progressive course and died after 43 days. The electroencephalogram showed the characteristic periodic triphasic complexes the day before death. Atrophy and a caudate high signal were seen in MRI. 14-3-3 protein was present in CSF. Mutation E200K in gene PRNP was found in her DNA lymphocytes. Neuro-pathology showed spongiform change and PrP deposition.

**Conclusion:** CJD may present with different psychiatric symptoms, which is why patients can be initially misdiagnosed and admitted to psychiatric wards. CJD should be considered in the differential diagnosis of patients who have focal neurological signs in addition to psychiatric symptoms. Repeated neurological examinations, EEG and cranial MRI may help in the diagnosis.

**P2116**

**THE DIFFERENTIATION OF THE SUBITEMS OF TURKISH MMSE ACCORDING TO CLINICAL STAGES IN ALZHEIMER TYPE DEMENTIA**

S. Dastan¹, G.G. Yener²

¹Department of Neural Sciences, Health Sciences Institute, ²Departments of Neurology and Social Sciences, Dokuz Eylul University, Balcova, Izmir, Turkey

**Background:** MMSE is the most common global cognitive test. The clinical stages of AD are characterised by losses in certain cognitive domains. Memory and orientation disorder are the earliest core symptoms, followed by visuo-spatial deficit while language is affected relatively later. These cognitive domains can be represented by the subitems of MMSE.

**Objective:** To investigate the changes in the subitems of Turkish version of MMSE according to the clinical stages in Alzheimer type dementia (AD).

**Methods:** The MMSE subitems include orientation, registration, mental control, memory, language and figure copying. GDS (Global Deterioration Scale of Reisberg) provides clinical staging in AD. We compared the MMSE subitems and GDS stages in 337 consecutive AD patient (176 females and 161 males) with at least 5 years of education, referred to Dokuz Eylul University Dementia Clinic between 1995 and 2001. Multiple logistic regression and Spearman rho were used for statistical analysis.

**Results:** Mean MMSE scores were 15 (SD=7.3) in females and 17 (SD=7.1) in males. There were 94 patients in the stage 3 and 130 in the stage 4 (in both stages females and males are equally numbered). Stage 5 and 6 consisted of 66 and 47 patients respectively. There was no relation between scores and age or education level. The correlation between the GDS staging and some MMSE subitems were observed. Orientation and memory were affected at the early stages.

**Conclusion:** Turkish version of MMSE subitems in AD population can predict the clinical stages.

**P2117**

**PRE-TEST RESULTS OF THE REVISED TURKISH VERSION OF STANDARDISED MINI MENTAL EXAMINATION TEST IN AN ELDERLY COMMUNITY DWELLING**

P. Keskinoglu¹, R. Ucku¹, G.G. Yener¹

¹Department of Public Health, ²Department of Neurology, Dokuz Eylul University, Izmir, Turkey

**Aim:** To examine the Turkish version of Standardised Mini Mental State Examination (sMMSE) some items were revised in an elderly community dwelling population as a pre-test.

**Methods:** The revised sMMSE of some items, such as orientation to time, orientation to place, phrase construction, phrase repetition and figure copying were changed according to educated and less educated older persons separately, was studied in 58 elderly, aged 65 years and older to be pre-test.

**Results:** Of the totally 58 elder subjects, 27 were educated 5 years and more, while 31 elderly were less educated, and mean age was 70.8 years. The total score, the scores of orientation to time and attention-calculation were significantly higher in the educated elderly. The score of recall was the lowest in both educated and less educated groups.

**Conclusion:** The revised sMMSE was a more understandable and simpler administrable test for educated and less educated elderly individuals. However, the reliability and validity of the revised test is necessary.

**P2118**

**EFFECTS OF A 6-MONTHS TREATMENT WITH DONEPEZIL AND RIVASTIGMIN ON RESULTS OF NEUROPSYCHOLOGICAL TESTS IN PATIENTS WITH ALZHEIMER’S DISEASE**

Sh. Gholizadeh¹, R. Abolfazli¹, T. Aavani²

¹Amiralam Hospital, Tehran University of Medical Sciences TUMS, ²Department of Biology, Faculty of Sciences, Shahid Beheshti University, Tehran, Iran

**Methods:** The MMSE subitems include orientation, registration, mental control, memory, language and figure copying. GDS (Global Deterioration Scale of Reisberg) provides clinical staging in AD. We compared the MMSE subitems and GDS stages in 337 consecutive AD patient (176 females and 161 males) with at least 5 years of education, referred to Dokuz Eylul University Dementia Clinic between 1995 and 2001. Multiple logistic regression and Spearman rho were used for statistical analysis.

**Results:** Mean MMSE scores were 15 (SD=7.3) in females and 17 (SD=7.1) in males. There were 94 patients in the stage 3 and 130 in the stage 4 (in both stages females and males are equally numbered). Stage 5 and 6 consisted of 66 and 47 patients respectively. There was no relation between scores and age or education level. The correlation between the GDS staging and some MMSE subitems were observed. Orientation and memory were affected at the early stages.

**Conclusion:** Turkish version of MMSE subitems in AD population can predict the clinical stages.

**P2119**

**POSSIBILITIES OF MEDICAL CORRECTION OF COGNITIVE IMPAIRMENTS (CI) WITH CEREBRO-VASCULAR DISEASE (CVD): ANALYSIS OF CASES FROM CLINICAL PRACTICE**

N.V. Kozachenko

Medical and Prophylactic City Polyclinic ?42, Rostov-On-Don, Russia
Rapid onset Dystonia Parkinsonism (RDP) is a rare genetic movement disorder recognised by sudden onset of bulbar and limb dystonia with parkinsonism; neuropsychiatric features are common. We report 2 unrelated cases. Case 1, a 20-year-old man, admitted with subacute onset of dystonia in upper, then lower limbs, facial and bulbar muscles, with generalised rigidity and slowing. Maximal disability was reached within 7 days. He remains mute and wheelchair bound 4 years after his initial symptoms. Case 2 is an almost identical presentation in a 20-year-old woman whose pyramidal and extra pyramidal signs were preceded by 2 weeks emotional lability. Neither was dopamine responsive. Both cases have a confirmed point mutation in ATP1A3 gene on chromosome 19q3. This gene has been shown to code for an integral protein in the neuronal membrane Na+/K+-ATPase pump. The inheritance is usually autosomal dominant with incomplete penetrance. We present 2 sporadic cases highlighting the importance of considering this diagnosis and screening for the gene despite the absence of a family history. We summarise the latest knowledge of the molecular genetics of this disorder.

P2122
SCREENING FOR FXTAS PREMUTATION IN ITALIAN PATIENTS WITH SPINOCEBELLAR ATAXIA
E. Cellini1, P. Forleo1, A. Ginestroni1, B. Nacmias2, A. Tedde1, S. Bagnoli1, S. Sorbi1, M. Mascalchi1, S. Piacentini1
1Department of Neurological and Psychiatric Sciences, 2Radiodiagnostic Section, Department of Clinical Physiopathology, University of Florence, Italy

Background and aims: Fragile-X-associated tremor/ataxia syndrome (FXTAS) is a novel late-onset neurological syndrome due to a premutation in the FMR1 gene. Males carrying the premutation develop progressive intention tremor, ataxia and cognitive decline, usually beginning between 50 and 70 years. Rarely female carriers manifest the disease, with a milder and later onset phenotype. Various screenings for FXTAS suggest that expanded FMR1 alleles may be considered a possible genetic cause of late-onset ataxia. We evaluated the presence of premutation carriers among male and female patients with sporadic ataxia without expansion into known SCA genes.

Methods: Clinical and genetic examinations were performed on 160 male patients with onset at age 30 to 84 years with sporadic pure ataxia and patients with ataxia associated with extracebellar features and in 195 female patients. Premutated allele lengths of the FMR1 gene were evaluated with fluorescent polymerase chain reaction.

Results: FMR1 premutation alleles with a repeated number greater than 55 were detected in 4 male probands (2.5%). 3 patients had typical FXTAS, and one patient had spastic paraparesis without clear symptoms of cerebellar ataxia and without the common signs seen at magnetic resonance imaging (MRI). One female carrying the FMR1 premutation had a late-onset and a mild disease course with ataxia and tremor.

Conclusions: Genetic analysis of the FMR1 gene could provide a reliable diagnostic tool for the definitive diagnosis of late-onset ataxias. Additional studies are needed to clarify the importance of premutation screening for FXTAS in patients with movement disorders or other associated atypical features.

P2123
TWO SPORADIC CASES OF RAPID ONSET DYSTONIA PARKINSONISM
A.S. Fitzpatrick, J.I. Morrow, V.P. Patterson
Neurology Department, Royal Victoria Hospital, Belfast, N. Ireland, UK

Movement disorders 2

P2124
TRANSCRANIAL SONOGRAPHY IN MOVEMENT DISORDERS
I. Galinovic, M. Budisic, M. Crnjakovic, D. Italo, I. Scuric, D. Radakovic, V. Vargek-Soler, V. Demarin
Department of Neurology, Sestre Milosrdnice University Hospital, Zagreb, Croatia

Background: So far, there is no reliable test that can clearly distinguish between various movement disorders. Therefore, the diagnosis is still based on the clinical examination. However, the misdiagnosis rate for the most common movement disorders – Parkinson's disease (PD) and Essential tremor (ET) – in the early stages is as high as 20–30% for PD and in about one of three patients in ET. We initiated these studies to assess the possibility of Transcranial sonography (TCS) to help differentiate PD from ET by measuring echogenicity of the substantia nigra (SN).

Patients and methods: Our study included 60 patients with PD, 30 patients with ET and 60 healthy controls. The TCS recordings were done in axial plane by standardized protocol by two independent investigators. SN was displayed, encircled, and measured two times. Mean area was calculated. Mann Whitney U test for inter-group comparison was applied.

Results: Patients with ET and PD had mean SN size of 0.15 cm² (+0.04) and 0.27 cm² (+0.06), which showed significant difference (p<0.001). In the control group bilateral combined mean SN size was 0.17 cm² (+0.06), which was significantly different from PD group (p<0.001), but not from ET group (p=0.240).

Conclusion: The measurement of SN by means of TCS is a valuable tool in the differentiation of movement disorders. Due to portability, lack of invasiveness and easiness of reproducibility, TCS might help in diagnosing PD or in differential diagnosis of doubtful clinical cases.

P2125
ESSENTIAL TREMOR IN CHILDREN
I. Kravou, I. Ben Youssef-Turki, A. Rouissi, N. Gouider-Khouja
Department of Paediatric Neurology, National Institute of Neurology, Rabta, Tunis, Tunisia

Introduction: Essential tremor (ET) is the most common idiopathic movement disorder. The disease is characterized by postural
tremor of the arm that may be present also during action and less frequently, tremor of the head, lips, voice, trunk and legs may be observed. ET is commonly familial and occurs in adulthood, with female predominance. However, early onset cases are more and more described. The aim of this presentation is to report 6 paediatric ET cases followed-up in our department, and to discuss clinical specificities and therapeutic possibilities.

Case reports and results: 6 children with 6 ET (5 males and 6 females, aged from 5 to 10 years) are reported. 4 children had consanguineous parents and 4 have familial history of tremor. All patients had postural tremor of arms, 3 had action tremor and one had associated myoclonic jerks. None had head or voice tremor. 3 patients had associated epilepsy and were under AE drug but tremor preceded AE drug prescription. Paraclinical investigations were negative. Various medications (Phenobarbital, propanolol, benzodiazepine, baclofen, piracetam) were used to treat tremor without significant improvement.

Comments: We found male preponderance and absence of head and voice tremor in children with ET. This finding is in accordance with the literature. Epilepsy was observed in half of the cases. Antiepileptic medication could exacerbate a pre-existent tremor. Male preponderance could be a result of a modification of disease expression by gender (i.e., age of onset). Investigation of new therapeutic strategies is necessary in children with ET.

P2126
PET IMAGING IN REFRACTORY GILLES DE LA TOURETTE SYNDROME AND STEREOTACTIC BILATERAL CAPSULOTOMY
Department of Neurology, Second Affiliated Hospital of Soochow University, Suzhou, China

Objective: To explore glucose metabolism changes of refractory Gilles de la Tourette syndrome (GTS) in PET scan and observe the effect of stereotactic bilateral capsulotomy for refractory GTS patients.

Methods: We examined the localized orbitofrontal and subtropical metabolic changes in FDG-PET by employing the region of interest (ROI) method in pre-operation and 6 months after operation. 7 cases refractory GTS underwent MRI guided stereotactic bilateral capsulotomy. The post-operation outcome of brain metabolic and clinical scales including tic severity, cognitive performance, and psychiatric status are under investigation by contrast to pre-operation so as to detect and evaluate the effects of capsulotomy for refractory GTS.

Results: There was a remarkable difference between the patients and control team in regional glucose metabolic changes (P <0.01). Moreover stereotactic capsulotomy induces localized orbitofrontal and subtropical metabolic changes and improves clinical symptoms in refractory GTS. No serious side effects happened except transient urpiclesia and weight loss in our study.

Conclusion: The metabolic abnormalities of FDG are universal and remarkable in PET to refractory GTS, especially in frontal and orbitofrontal lobe and cingulated cortices and caudate. FDG-PET changes demonstrated that capsulotomy do decrease remarkably regional hypermetabolism, which might be related to mechanism of surgical treatment of refractory GTS. MRI guided stereotactic capsulotomy is a precise, safe, very effective therapy in some ways for refractory GTS. It is promised to improve the symptoms of GTS as well as OCD, anxiety and depression.

P2127
EFFECTS OF ANODAL TRANSCRANIAL STIMULATION ON THE EXCITABILITY OF MOTOR CORTEX IN HEMICEREBELLECTOMIZED RATS
N. Oulad Ben Taib1, M. Manto1
1Hopital Saint-Pierre, 2Departement De Neurologie, FNRS, Bruxelles, Belgium

Anodal transcranial stimulation (ATS) induces changes of cortical excitability. Anodal DC stimulation produces in particular sustained neuronal membrane depolarisation. One of the elemental deficits associated with hemicerebellotomy is a decreased excitability of the contralateral motor cortex, likely due to a loss of excitatory drive exerted by the cerebellolothalamocortical pathway. The weakened excitability is associated with an inability to tune corticomotor responses in a context of sustained peripheral stimulation. This is considered to be involved in the pathogenesis of learning deficits. We analysed the effects of ATS on motor cortex excitability in rats undergoing hemicerebellotomy. Left cerebellar hemisphere was removed surgically in 5 male adult Wistar rats. Histological verification of unilateral cerebellar ablation was performed for each rat. Amplitudes of corticomotor responses in left gastrocnemius muscle were compared before and after 20 minutes of ATS on right motor cortex at 0.4 mAmp. Control values obtained by stimulation of the left motor cortex were 754.8±83.4 μV (median: 779 μV). Before ATS, amplitudes of right corticomotor potentials were 611.60±60.7 μV (median: 599.0 μV). Following ATS, amplitudes raised to 711.2±61.7 μV (median: 734 μV; p=0.033). These results show that ATS may improve one of the deficits in motor cortex responses contralaterally to a unilateral cerebellar ablation. It is likely that ATS acts upon intra-cortical circuits targeted by thalamocortical projections. ATS could be considered in attempts to modulate the deficits in the cortical sensorimotor network excitability associated with acute cerebellar lesions.

P2128
A WEARABLE EXOSKELETON FOR ANALYSIS AND TREATMENT OF ESSENTIAL TREMOR
S. Camut1, E. Roccoi2, J. Pons3, J.M. Belda3, M. Manto1
1Departement de Neurologie, ULB, Bruxelles, Belgium, 2IAI-CSIC, Madrid, 3IBV, Valencia, Spain

Essential tremor (ET) represents the most common movement disorder in the elderly. Most patients exhibit combinations of postural/kineti c tremor. Despite advances in drug therapy and surgery, more than 40% of patients with ET report disabilities. Drugs currently used, including primidone or propanolol, may induce side effects and surgery is not without risk. We describe a new method for the simultaneous assessment (no force applied) and treatment (bio-mechanical loading) of ET. A motor providing effective viscosity is fixed on a wearable orthesis applying dynamic forces on wrist and elbow. The motors are controlled by a PC controlling in real time the position and rate of rotation of joints. The angular velocity information is used to compute the reference mass and the damping characteristic. The exoskeleton was assessed in 6 patients presenting ET and exhibiting a postural/kinetic tremor in upper limbs at intensities of 2/4 to 4/4 despite regular use of medications (mean age of 72.3 years). Range of tremor suppression varied from 2.9% (percentile 5) to 78.5% (percentile 95) in relation to energy in the monitoring mode. The exoskeleton was active both on kinetic and postural tremor. Damping was more effective in advanced tremor. Dominant tremor frequencies remained stable despite the reduction in amplitudes of tremor. Mean tremor energy reduced from 55.49 to 15.66 rad2/sec3 (p=0.018). This new technique is non invasive.
providing information on interactions between kinematics, dynamics and tremor genesis. The exoskeleton effectively reduces tremor amplitude, especially in patients with severe ET.

P2129
THE PSEUDOSCLEROTIC TYPE OF WILSON’S DISEASE (WD) IS ASSOCIATED WITH THE MISSENSE MUTATION R616Q IN THE ATP7B

V. Mihaylova1, T. Todorov2, O. Kosseva1, Z. Krustev1, I. Kotev1, G. Georgieva1, S. Sarafov1, I. Kremensky2, I. Tournev1
1Department of Neurology, University Hospital, 2Laboratory of Molecular Pathology, Specialized Hospital of Obstetrics and Gynaecology, Sofia, 3Department of Gastroenterology, University Hospital, 4Department of Gastroenterology, University Hospital “St.Marina”, Medical University Varna, 5Department of Gastroenterology, University Hospital, Bulgaria

Wilson’s disease is an autosomal recessive disorder of copper metabolism presenting with a variety of symptoms, commonly as liver and/or neuropsychiatric disease. At least 300 mutations in WD gene (ATP7B) were described. The genotype-phenotype correlations are complicated because of the rarity of some mutations and the large number of compound heterozygotes. We studied 127 Bulgarian patients diagnosed as having WD. Detailed history, physical and neurological examination, biochemical studies of copper metabolism, ultrasound abdominal scanning, slit-lamp examination, neuropsychological testing, MRI and/or CT of the brain were performed. Molecular genetic testing by means of SSCP analysis followed by direct sequencing was carried out in all patients. Out of 124 patients with genetically verified WD diagnosis, 9 were found to have the missense mutation R616Q on one allele, with two further cases found to be R616Q homozygotes. Ten of R616Q patients presented with late onset of neurologic and/or psychiatric symptoms. The neurological symptoms were invariably cerebellar, with only one patient having Parkinsonism in addition to the cerebellar ataxia. All of the R616Q patients had Kayser-Fleischer rings and normal or slightly reduced ceruloplasmin levels. Though the limited number of patients, our findings suggest that the R616Q mutation is associated with pseudosclerotic type of WD. Moreover, only ataxia and dysarthria were found in the two R616Q homozygotes. After exclusion of the common ATP7B mutations, testing for R616Q should be applied to WD patients presenting with pseudosclerosis.

P2130
INCIDENCE OF PARKINSON’S DISEASE AND SEVERITY OF PARKINSONISM AND DISABILITY IN PATIENTS WITH EARLY, UNTREATED DISEASE – THE NORWEGIAN PARKWEST STUDY

B. Mueller1,2, G. Alves3, K. Herlofsen, I. Hoejen-Esch, W. Telstad, J.P. Larsen1,2, O.B. Tysnes1,2, G. Alves1
1Department of Neurology, 2Section for Neurology, Institute for Clinical Medicine, Haukeland University Hospital, Bergen, 3The Norwegian Centre for Movement Disorders, Stavanger University Hospital, Stavanger, Norway

Background and aims: Parkinson’s disease (PD) is increasingly recognized to be a multisystem brain disease leading to both motor and a variety of non-motor problems. However, knowledge on the prevalence and severity of non-motor symptoms in patients with early, untreated disease is limited. The aim of this study was to study the frequency and severity of various non-motor symptoms in a representative cohort of patients with incident and untreated PD.

Methods: A prospective longitudinal study of patients with incident Parkinson’s disease, the Norwegian ParkWest study, has been enrolled in four counties of South-Western Norway, comprising a total population of 1,061,000 inhabitants. Inclusion of all patients with incident PD within the study area between November 1st, 2004 and August 31st, 2006 was intended. The study is approved to last over 10 years, with regularly follow-up visits and comprehensive examinations. The following instruments were used to clinically assess the frequency and severity of different non-motor symptoms at baseline: Montgomery and Aasberg Depression Rating Scale (MADRS), Mini-Mental State Examination (MMSE), Starkstein Apathy Scale (SAS), Neuropsychiatric Inventory (NPI), Stavanger Sleepiness Questionnaire (SSQ), Epworth Sleepiness Scale (ESS), Parkinson’s disease Sleep Scale (PDSS), Fatigue Severity Scale (FSS), and the Unified Parkinson’s disease Rating Scale (UPDRS) subscale I. In addition, information was obtained on urinary function, constipation, pain and symptomatic orthostasis using clearly defined 5-point scales.

Results: Baseline data on the frequency and severity of various non-motor problems in a representative cohort of patients with incident and untreated PD will be presented.

P2132
CLINICAL AND RADIOGRAPHIC FINDINGS OF NEURODEGENERATION WITH BRAIN IRON ACCUMULATION: DISTINCTION FROM OTHER JUVENILE ONSET DEGENERATIVE DISORDERS

M.F. Oztekin1, N. Subutay Oztekin1, G. Orhan1, F. Ak1
1Neurology Department, 2Neurology Department, SB Numune Education and Research Hospital, Ankara, Turkey
Objective: Neurodegeneration with brain iron accumulation (NBIA) is an autosomal recessive disorder characterized by dystonia, parkinsonism, and iron accumulation in the brain. In this study, we report the clinical and radiographic features of 3 patients with NBIA syndrome and emphasize the importance of accurate diagnosis for accurate treatment.

Background: The diagnosis of NBIA syndrome applies to a spectrum of disorders that share the common features of neurodegeneration and iron accumulation in the brain. Recently it was discovered that many cases of NBIA syndrome result from mutations in a gene located on chromosome 20p13. The culprit gene (PANK2) encodes a novel pantothenate kinase. 

Method: We report the clinical findings of 3 patients 28, 19 and 43 years old consecutively whose diseases started with extrapyramidal symptoms in the first decade of their life progressing further relentlessly and without having appropriate treatment.

Results: All the patients had pyramidal signs along with extrapyramidal symptoms, and MRI findings consistent to NBIA disease. The two older patients 28 and 43 years of age had also parkinsonian rigidity. One patient had a positive family history. All other causes of neurodegenerative disorders are excluded by laboratory methods.

Conclusion: NBIA syndrome can sometimes be misdiagnosed as juvenile Parkinson’s disease. For this reason early onset cases with dystonia intellectual impairment must be carefully evaluated and PANK2 gene should be analysed. Parkinsonism is seen predominantly in adult-onset patients whereas dystonia seems more frequent in the earlier-onset cases.

P2133
QUALITY OF SLEEP, RLS SYMPTOMS AND DEPRESSION IN PATIENTS WITH SPINOCEREBELLAR ATAXIA

M. Rakowicz, A. Wierzbicka, A. Wichaök, R. Rola, M. Miewiadomska, E. Zdzienicka, A. Sulek-Piatkowska, M. Wieclawska, T. Jakubczyk, W. Jarzątky

Spinocerebellar ataxia (SCA) are autosomal dominant neurodegenerative disorders. Recently, a relation of restless legs syndrome (RLS) with SCA has been noticed. Aim of the study was to evaluate RLS symptoms, sleep quality and mood in patients with SCA.

Method: 36 SCA1 and 19 SCA2 patients molecularly confirmed in mean age 44.2±12.5 years and with mean disease duration 9.7±6.4 years were investigated. The International Cooperative Ataxia Rating Scale (ICARS), sensory and motor neurography, Athens Insomnia Scale (AIS), rating scale for the severity of RLS (IRLSSG), Beck Depression Inventory (BDI) were used as assessment methods. Additionally actigraphy was performed in 24 randomly selected patients.

Results: Mean ICARS score amounted to 34.2±16.5. Depressive symptoms (mild to severe; BDI>14) were observed in 24 patients. Moderate insomnia was found in eight patients (AIS>6), severe in 13 patients (AIS>10). Nine subjects reported RLS symptoms as severe, 19 patients as moderate. However, only three patients reported either complete or almost complete relief of RLS symptoms while moving, further 16 patients reported only moderate or slight relief. Actigraphy revealed periodic leg movements in sleep (PLM-Index >10/h) in 29% of examined patients.

Conclusion: Patients with SCA frequently suffer from insomnia and limb restlessness. However, the diagnostic criteria for RLS are rarely fulfilled. In most of the patients the limb restlessness seems to result from sensory-motor neuropathy and depressive reaction. Sleep quality in SCA patients may be improved by neurological rehabilitation, increasing of daytime activity and effective treatment of depression.

Supported by 6th EU FP EUROSCA Grant Nr LSHM-CT-2004-503304.

P2134
GENE EXPRESSION PROFILING IN THE NIGRO-STRIATAL SYSTEM OF UNILATERALLY 6-HYDROXYDOPAMINE LESIONED RATS UNDER VARIOUS ROTIGOTINE TREATMENT CONDITIONS

E. Gruenblatt, D.K.A. Scheller, W.J. Schmidt, M. Gerlach, P. Riederer

Background and aims: Continuous dopaminergic stimulation is thought to reduce the prevalence of dyskinesia. Rotigotine, a non-ergolinic dopamine agonist developed for the treatment of idiopathic Parkinson’s disease, is administered transdermally to provide continuous drug delivery. This study investigated the gene expression pattern in striatum (STR) and substantia nigra (SN) under continuous or pulsatle drug administration.

Methods: Rats with unilateral nigrostriatal 6-OHDA-induced lesions were treated for 10 days with either saline, L-DOPA/benserazide (10/15 mg/kg), continuous rotigotine (1 mg/kg every 2nd day, retroformulation) or pulsatle rotigotine (1 mg/kg saline BID). A Rat Neurobiology U34 gene chip (Affymetrix) was used to study the gene expression in the STR and SN. Quantitative real-time RT-PCR (qPCR) was used for confirmation of changes of representative genes.

Results: Pulsatile administration of L-DOPA or rotigotine caused sensitization of locomotor activity whereas continuous administration did not. Analogously, pulsatle L-DOPA or rotigotine significantly changed the expression of 15/11 genes in the SN/STR, respectively, which where not changed with continuous rotigotine. Using qPCR a significant down regulation of the neurotrophin 3 (NT3) mRNA was confirmed for pulsatle rotigotine. For continuous rotigotine, the lack of changes of genes selected for qPCR was confirmed.

Conclusion: The differential gene expression in SN and STR of sensitized rats suggests their potential involvement in the generation of dyskinesias. The lack of changes of these genes under the continuous treatment suggests that continuous receptor stimulation normalizes the expression pattern. In particular, the response of the NT3 gene points to a potential mechanism.

P2135
STRIATAL FP-CIT UPTAKE CORRELATES WITH CLINICAL PHENOTYPE OF EARLY PARKINSON’S DISEASE


Background and aims: In idiopathic Parkinson’s disease (PD), a tremor-dominant type (TDT), an akinetic-rigid type (ART), and a mixed type (MT) are distinguished. We compared cerebral [1-I23]FP-CIT SPECT in the PD subtypes.
Method: We studied 67 PD patients Hoehn and Yahr stage 1: 26 with ART, 19 with MT, 22 with TDT. We measured the ratios putamen / occipital lobe binding and caudate nucleus / occipital lobe binding. Parkinsonian motor symptoms were quantified by UPDRS motor scale.

Results: In both putamen and caudate nucleus contralateral to the clinically affected body side TDT patients showed a significantly higher FP-CIT uptake than ART or MT patients (ANOVA; p<0.01). Contralateral putamen and caudate nucleus FP-CIT uptake correlated significantly with severity of rigidity (p<0.01) and hypokinesia (p<0.01) but not with severity of resting or postural tremor (p>0.05).

Conclusions: The missing correlation between striatal FP-CIT uptake and tremor suggests that further systems besides the nigrostriatal dopaminergic system may contribute to generation of parkinsonian tremor.

P2136
POTENT EFFECTS OF LACOSAMIDE IN RODENT MODELS FOR CNS DISORDERS
T. Stoehr, J. Freitag
Department of Pharmacology and Toxicology, Schwarz Biosciences, Monheim, Germany

Purpose: Lacosamide (LCM) is an investigational anticonvulsant drug currently undergoing phase III clinical testing for the treatment of epilepsy. Since anticonvulsant drugs are being used for the treatment of a variety of other CNS disorders we profiled LCM in different rodent models. Essential Tremor is a prevalent movement disorder which is commonly treated with anti-epileptic drugs (e.g. primidone, topiramate) which have proven clinical efficacy. The potential of LCM was thus assessed in the hamaline model for essential tremor. Anti-epileptic drugs have also proven clinical efficacy for the treatment of different forms of dyskinesia. In order to screen for potential antidyskinetic properties LCM was tested in a simple animal model with predictive validity for tardive dyskinesias (reserpine test).

Methods and results: A single administration of harmaline induced tremors which lasted for at least 120 min. The positive reference compounds propanolol and primidone significantly reduced the intensity of harmaline-induced tremors, thus validating the model. Lacosamide (0.3–30 mg/kg i.p.) reduced the intensity of harmaline-induced tremors in a dose-dependent manner. At the highest doses tested, the maximal efficacy was higher than that of propanolol and comparable to that of primidone. Dyskinesias in the form of vacuous chewing movements were induced by two injections of reserpine. Lacosamide (30 mg/kg) induced moderate anti-dyskinetic effects in this test.

Conclusions: The present results show that LCM was effective in animal models for essential tremor and tardive dyskinesia. Thus, it is a new candidate drug worth further testing in clinical trials.

P2137
TREATMENT OF CEREBRAL SPASTIC INFANTILE PARALYSIS BY TRANSCUTANEOUS ELECTRICAL STIMULATION OF THE SPINAL CORD
A.A. Sufianov1, A.G. Shapkin1, G.Z. Sufianova2, M.V. Taborov1, Yu.G. Shapkin1, O.V. Koroleva1
1East-Siberian Scientific Centre of Siberian Branch of Russia, 2State Medical University, 3Institute of Solar-Terrestrial Physics of the Siberian Branch, The Russian Academy of Science, Irkutsk, Russia

Background and aims: The purpose of work was development and a clinical estimation of a method transcutaneous electrical stimulations of the spinal cord (ESSC) at cerebral spastic infantile paralysis.

Methods: 22 persons in the age of from 2 till 14 years participated in our study. In the neurologic status at 72% of patients the spastic diplegia was verified. The electrical stimulation was executed by a bipolar technique with using of impulse current with frequency of 20 Hz. Electrodes for an electrical stimulation placed in bottom thoracal and top lumbar parts (in interspinal intervals). All of the patients had 10 sessions of ESSC.

Results: Prior to the beginning of treatment the average level of neurologic disturbances, according to a Ashworth spasticity scale was been 2.8±0.2 a point, a degree of locomotor functions disturbance (Arens scale) –2.4±0.4 a point. After the lead treatment was observed spasticity reduction up to 1.25±0.13 points (p<0.001), improvement of locomotor functions up to 3.7±0.3 points (p<0.05). According to registration of spontaneous bioelectric activity of spinal cord decrease of total amplitude of electospinogramm on 60.5% from an initial level (p<0.05) was recorded, that signifies normalization of neurodynamic processes in the nervous tissue of the spinal cord.

Conclusions: ESSC is a highly effective and non-invasive therapeutic method of correcting motor disturbances in cerebral palsy.

P2138
OLFACTORY DYSFUNCTION IN PARKINSON’S DISEASE: AN FMRI STUDY
A. Takeda, A. Kikuchi, T. Hasegawa, N. Sugeno, N. Saito, Y. Royama
Department of Neurology, Tohoku University Hospital, Sendai, Miyagi, Japan

Objective: To study olfactory impairments in Parkinson’s disease (PD) objectively, we developed an functional MRI system, which can visualize brain activation by olfactory stimuli.

Background: Olfactory dysfunction in PD was firstly described several decades ago. Since then, a number of studies have reported that olfactory impairments are one of the earliest symptoms in PD. However, all smell tests used in previous studies depend on subjective answers by examinees and on “sniffing”, which may be impaired in PD as one of motor symptoms.

Methods: We developed an fMRI system, which can visualize brain activation by olfactory stimuli during natural breathing. Each odorant exposure consisted of the 30 seconds of stimulus-on and 30 seconds of off-phase with continuous air flow. Six times of exposures were repeated each of odorous stimuli. The data obtained were analyzed and visualized by using the standard parametric mapping technique (SPM99). All procedures were approved by the ethical committee and a written-informed consent was obtained from all participants.

Results: 5 patients and age-matched controls voluntarily participated in the study. In healthy controls, significant brain activation was observed mainly in frontal lobes, but in PD patients, only a trace-level activation was detected by the same olfactory stimuli.

Conclusions: This study suggests that the olfactory dysfunction in PD is due to impaired olfactory perception itself. Recent studies demonstrate that the olfactory impairments may precede the onset of motor symptoms. Olfactory examinations combined with routine tests and this fMRI study can be applied for a possible pre-symptomatic diagnosis of PD.

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
P2139
THE ABNORMAL AGGREGATION OF ALPHASYNUCLEIN INDUCES AUTOPHAGIC PROGRAMMED CELL DEATH IN PC12 CELLS
Y.P. Yang1,2, K.Y. Liu1, J.J. Qian1, Y.B. Cheng1,2, C.J. Mao1, C.F. Liu1,2
1Department of Neurology, Second Affiliated Hospital of Soochow University, 2Laboratory of Aging and Nervous Diseases, Soochow University, Suzhou, China

Objective: We aim to observe the effect of mutant α-Synuclein (A30P) in autophagic programmed cell death by transfected PC12 cells and explored its probable role and pathway in PD.

Methods: We chiefly constructed definite PC12 cells which were transfected mutant α-Synuclein (A30P) and administered MPTP, Rapamycin and Wortmannin to PC12 cells and transfected PC12 cells with mutant α-Synuclein. We not only detected reproductive activity of cells with MTT method but also observed the ultrastructural changes of cells and expression of α-Synuclein in different circumstances by Transmission electron microscopy (TEM), Western Blotting and Real-time PCR. Moreover, we employed immunofluorescence method to mark both α-Synuclein and Atg 8 simultaneously in order to detect the aggregation of α-Synuclein and occurrence of autophagy in transfected cells.

Results: Mutant α-Synuclein (A30P) leading to PC12 cells death by means of autophagy involves α-Synuclein accumulation, membrane lipid oxidation, and loss of plasma membrane integrity. Mutant α-Synuclein (A30P) mediates the toxicity of MPTP. Rapamycin, an inducer of autophagy, reduces the aggregation of α-Synuclein in transfected cells and protects against neurodegeneration in a mice model of Parkinson disease. Meanwhile, Wortmannin, an inhibitor of autophagy, promotes the aggregation of α-Synuclein in transfected cells and induces cells to die.

Conclusion: The abnormal aggregation of α-Synuclein induces autophagic programmed cell death in PC12 cells and mutant α-Synuclein (A30P) mediates the toxicity of MPTP. Meanwhile, Rapamycin may reduce the aggregation of α-Synuclein in transfected cells by activation of autophagic pathway.

P2140
CERVICAL MOVEMENT CHARACTERISTICS IN CERVICAL DYSTONIA: A PROSPECTIVE STUDY
D. Zegers de Beyl1, V. Feipel1, P. Salvia1
1Service Neurologie, Hôpital Erasme, 1Laboratoires d’Anatomies, Université Libre de Bruxelles, Belgium

Background: Many studies concern clinical characteristics and treatment results of patients with cervical dystonia (CD). Quantitative studies on neck movements in patients with CD are very rare.

Objective: To measure range and velocity of neck movements and associated involuntary movements in patients with CD who perform successively neck rotation, flexion/extension and lateral bending movements at spontaneous speed. Clinical evaluation was done with TWSTR scale.

Patients and methods: 34 consecutive patients with CD were prospectively studied. The results were compared to a control group of 29 age matched normal subjects. Quantitative measures of cervical movements were measured with three-dimensional electromanometry.

Results: Range of movements of patients were moderately but significantly reduced for flexion/extension and rotation. A very robust and highly significant reduction of maximal movement velocity was seen for all the movements. The reduction of movement velocity was not correlated to the severity of dystonia or to the pain score of the TWSTR scale. In 16 patients, in whom recordings were repeated after botulinum toxin injections and physiotherapy, maximal speed of movements remained unchanged despite improvement of clinical rating.

Conclusion: Reduction of speed of voluntary neck movements in CD patients is not studied in clinical scales like the TWSTR and hitherto non recognized. It was the most robust abnormal finding in this prospective study. It seems not correlated to dystonia severity and neck pain. It is possible that it reflects the disturbed regulation of agonist and antagonist muscles in patients with dystonia.

P2141
GAIT DISORDERS: STEP VARIABILITY FACTOR (SVF) AS DIAGNOSTIC CRITERION IN PARKINSON’S DISEASE (PD) AND VASCULAR PARKINSONISM (VP)
V.G. Abramov, D.V. Pokhabov
Krasnoyarsk’s State Medical Academy, Centre of Neurology of “Siberian Regional Medical Centre”, Krasnoyarsk, Russia

Generally, while walking flat surface, regular conditions, a person’s step length is constant and follows normal distribution pattern, optimizing power expenses. With different neurological disorders, including PD and VP gait pattern changes. For PD, disorders of walking initiation, step length decrease, freezing of gait are typical. For VP there are even more significant walk initiation disorders, however, after few small steps, step length increases, but remains variable. By continuous studying the variability of step, objectification of these changes can be reached.

Goal: Investigate step variability for PD and VP, determine this parameter’s usefulness.

Materials and methods: We have investigated gait of 30 PD patients, aged 66±1.8 years; 30 VP patients, aged 71±2.5 years; 30 clinically healthy people, aged 69±1.2 years (normal group for aged); 20 clinically healthy people aged 22±1.7 years, (normal group for young) using computer hardware-software complex “Dorozhka” which measures every step length. We’ve analyzed average step length (ASL) and relative parameter, we called step variability factor (SVF) calculated by formula.

P2142
PAIN AND DEPRESSION IN PARKINSON’S DISEASE
S. Albu1, S. Odobescu1, G. Pavlic1, I. Moldovanu1
1Department of Neurology, State Medical and Pharmaceutical University “Nicolae Testemitanu”, 1National Institute of Neurology and Neurosurgery, Chisinau, Moldova

Background and aims: Patients with Parkinson’s disease (PD) frequently experience pain symptoms. Its origin may be related to PD or to existing comorbidity. The association of depression in these patients causes severe disability. The goal of this study was to evaluate the pain pattern in PD and its correlation with depression.

Methods: Thirty patients with PD affected by severe pain were included in the study. A clinical exam (including UPDRS) and neuroimaging studies have been performed. The pain was evaluated by an original questionnaire comprising aspects of topography, nature, evolution, intensity of pain (measured with Visual-Analogical Scale) and its sensitivity to drug treatment. The depression syndrome was estimated by Hamilton Depression Rating Scale.

Results: The patients were divided in 2 groups. The first included 12 patients with parkinsonian pain (PP) localized on the affected regions, varying in character and intensity. We observed an important alleviation of pain in 9 patients under antiparkinsonian
therapy, but no response to analgesics. 18 subjects experienced non-PP caused by: spondylosis, migraine, myofascial syndrome, with an evident correlation between the pain nature and comorbid conditions responding to their specific treatment. The depression syndrome has been observed in 5 patients with PP and 7 cases with non-PP in advanced stages of PD. They reported more severe pain, associated with sleep disorders.

**Conclusion:** The clinical data suggest the complexity of pain symptoms in PD which can be successfully managed adjusting their specific treatment. The depression syndrome worsens the general status of the patients and also requires treatment.

**P2143**

**TOPIRAMATE IN THE TREATMENT OF DYSTONIA**

M. Arnaoutoglou1, S.E. Kapsali1, E. Avdelidou1, T. Tihalas1, G. Spanos2, F. Sedaghat1, V. Kosta1, N. Arnaoutoglou1, G. Xiromerisiou1, E. Kalliolia1, A. Psarakou-Gotzamani1, S.J. Baloyannis1

**Background:** Topiramate was introduced as a new multipotent antiepileptic drug. Since then its application was extended to other neurological diseases (essential tremor, idiopathic intracranial hypertension etc.) suggesting that there is potential for future application in other CNS disorders.

**Case reports:** We present two case reports of dystonic tremor who responded to topiramate treatment. Case A, male, aged 62, presented with a two years history of dystonic posturing and tremor of the right hand during writing (writer's cramp), resulting in inability of producing a legible text. Case B, male, aged 65, presented lower limb tremor in the erect position (orthostatic tremor). Neurological examination of patients A and B, apart from focal and segmental tremor and dystonia respectively, was unremarkable.

**Neuroimaging** (Brain MRI, SPECT synaptic dopamine transporter imaging, 123I- DATSCAN) was normal. Both patients were treated with low doses of topiramate (100 mg/day), with minimal and transient side-effects (mild sedation). Both patients responded to treatment with significant amelioration of dystonia and tremor, resulting to improved daily activity scales.

**Conclusion:** Although our study is a presentation of case reports our results are indicative that topiramate treatment in dystonia and dystonic tremor is efficient and well tolerated.

**P2144**

**DELAYED HEMICHOREA FOLLOWING CORTICAL INFARCTION**

J.S. Baik, J.H. Park, J.Y. Kim, S.W. Han

**Department of Neurology, Inje University, Sanggye Paik Hospital, Seoul, South Korea**

**Background:** Chorea due to vascular event is less than 1% of patients with acute stroke. Most of them have lesions of the basal ganglia and adjacent white matter in the territory of the middle or posterior cerebral artery. We present a case with delayed hemichorea following cortical infarction.

**Case:** A 67-year-old woman presented with hemiparesis on the left side suddenly because of hemorrhagic infarction on the right fronto-temporal lobe. Eight days later, her weakness was improved, but she noticed involuntary movement on the paretic lower limb. Those movements were unpredictable, brisk with element of flexion or rotation and were aggravated by voluntary upper limb movement. Brain SPECT showed hypoperfusion on right fronto-temporal cortex and basal ganglia.

**Conclusion:** This case has a time interval between onset of stroke and initiation of involuntary movement and chorea of lower limb was aggravated by voluntary movement of upper limb. We consider that cortical lesion with basal ganglia abnormality on blood flow study was associated with delayed hemichorea.

**P2145**

**UNILATERAL HAEMORRHAGE IN GLOBUS PALLIDUM EXTERNUM IMPROVING THE PARKINSONIAN SYMPTOMATOLOGY BILATERALLY. A CASE REPORT**

M. Balaz, I. Rektorova, I. Rektor

**Department of Neurology, St. Anne University Hospital, Brno, Czech Republic**

We report the case of a 75-year-old patient with unilateral basal ganglia lesion caused by haemorrhage to the external globus pallidum. The lesion caused bilateral improvement of parkinsonian symptomatology with only minimal neurological sequelae. Lesion mimicking the DBS STN surgery with lasting lesional effect (stable improvement in UPDRS III at 3 and 6 months after the haemorrhage) with minimal residual paresis allowed substantial decrease of dopaminergic medication. We suppose that the onset of choreatic dyskinesias observed after the brain haemorrhage in the patient with a stable dose of dopaminergic treatment suggested the beneficial effect of the lesion on the parkinsonian symptomatology.

**P2146**

**DIAGNOSIS OF DOPA-RESPONSIVE DYSTONIA IN CHILDREN**

M.Yu. Bobylova1, S.V. Mikhailova1, I.D. Fedonuk1, E.S. Ilina1, L.P. Grinio1

1Department of Child Neurology, Russian State Medical University, 2Russian Child Clinic, Moscow, Russia

We surveyed 11 patients (aged 2–5) with dystonia of limbs and trunk and delay of motor development from birth (initial diagnosis was cerebral palsy), without epileptic disorders (method excluding 24-hour EEG-monitoring). All patients had low levels of urine catecholamines (dopamine, epinephrine, vanillylmandelic acid, norepinephrine; homovanillic acid) by chromatography. Activity of tyrosine hydroxylase in the lymphocytes was decreased. The patients’ MRI were normal. The therapy with levodopa (10–15 mg/kg per day) was highly effective. The motor skills of the patients improved; 8 from 11 patients have taken their first step and have spoken their first word. We believe the research of tyrosine hydroxylase activity may serve as a screening for dopa-responsive dystonia in children with hyperkineties and delay of motor development. Such patients should be searched for frequent mutations of tyrosine hydroxylase gene.

**P2147**

**SECONDARY CHRONIC MULTIPLE TICS**

M.Yu. Bobylova, K.V. Zapolsky

**Department of Child Neurology, Russian State Medical University, Moscow, Russia**

We observed 140 patients (90 male, 50 female; age 5–15, mean age 12.5±1.2 years) with tics (and diagnostic criteria for “chronic multiple tic disorder”) during 6 years. The majority of the patients
(n=124, 89%) had secondary tics: Depression, n=13 (6 m, 7 f); ADHD, n=12 (9 m, 3 f); Schizophrenia, n=12 (9 m, 3 f); Mental retardation, n=11 (8m, 3f); Autism n=2 (2 m); Neurofibromatosis n=3 (1 m, 2 f); Disgenesia of cerebellar vermis n=20 (12 m, 8 f); Sandifer syndrome n=2 (1 m, 1 f); Torsion dystonia n=22 (10 m, 12 f); Gallavorden-Spats disease n=5 (3 m, 2 f); paroxysmal dyskinesia n=3 (1m, 2 f); Tourette’s syndrome n=3 (2m, 1 f); Essential tremor n=4 patients (4 f); Huntington’s disease n=1 (1 f); an encephalitis n=3 (1 m, 2 f); head trauma n=5 (4 m, 1 f); a hemicraniectomy of the basal ganglia n=3 (2m, 1f).

P2148
CO-MEDICATION WITH ANTI-MEMETIC DOMPERIDONE DOES NOT AFFECT STEADY-STATE PHARMACOKINETICS OF TRANSDERMAL ROTIGOTINE
M. Braun, W. Cavello, R. Horstmann
Department of Clinical Pharmacology, Schwarz Biosciences GmbH, Monheim am Rhein, Germany

Background: Rotigotine (Neupro®), a non-ergolinic D3/D2/D1 dopamine agonist is being developed as a once-daily transdermal delivery system for the treatment of Parkinson’s disease and Restless Legs Syndrome. The peripheral dopamine antagonist domperidone is widely used in the prophylaxis and treatment of nausea and vomiting in patients using dopaminergic therapy. This clinical trial investigated potential effects of domperidone on steady-state pharmacokinetics, safety and tolerability of transdermal rotigotine.

Methods: Steady state pharmacokinetics of rotigotine (4.5 mg/10 cm²; nominal delivery dose: 2 mg/24 h) was studied in the absence and presence of oral domperidone (10 mg t.i.d.) in an open-label, treatment-sequence randomized, crossover trial in 16 healthy male subjects. The following PK parameters were assessed: Cmax,ss, AUC (0–24), ss, tmax, ss, t1/2, renal clearance (CLR) and amount of drug excreted in urine (Ae). Safety and tolerability were evaluated by adverse events, vital signs, ECG, physical examination, laboratory tests and skin assessment.

Results: The mean concentration-time profiles of rotigotine were similar with and without domperidone co-medication. There was no statistical difference for the primary variables Cmax,ss and AUC (0–24),ss of rotigotine with or without domperidone co-medication. The 90% confidence intervals for ratios of geometric means for Cmax,ss and AUC (0–24),ss were within the acceptance range for bioequivalence (0.8; 1.25). There was no relevant change in tmax, ss, t1/2, CLR and Ae. Rotigotine was well tolerated in the absence and presence of domperidone.

Conclusions: There is no evidence for interactions of domperidone on bioavailability and steady-state pharmacokinetics of rotigotine.

P2149
IMPACT OF MODERATE IMPAIRMENT OF HEPATIC FUNCTION ON THE STEADY-STATE PHARMACOKINETICS OF TRANSDERMAL ROTIGOTINE
W. Cavello, M. Braun, R. Horstmann
Department of Clinical Pharmacology, Schwarz Biosciences GmbH, Monheim am Rhein, Germany

Background: Rotigotine (Neupro®), a non-ergolinic D3/D2/D1 dopamine agonist, is being developed as a once-daily transdermal delivery system for Parkinson’s disease. In these patients of older age the effects on impaired hepatic function of pharmacokinetics have to be considered.

Methods: Steady-state pharmacokinetics of transdermal rotigotine (3 days, 4.5 mg/10 cm² once-daily, nominal delivery dose: 2 mg/24 h) was studied in a clinical trial in subjects with moderate hepatic impairment (Child-Pugh score B; mHI; n=8) compared to healthy subjects (HS; n=8).

Results: Plasma concentration time profile was similar in subjects with mHI and in HS. The statistical comparison (ANOVA) of Cmax,ss and AUC(0-24),ss in HS vs. subjects with mHI resulted in point estimates close to 1. Renal clearance of unconjugated rotigotine was similar in both groups while total body clearance was 15% higher in subjects with mHI. Plasma concentrations of total rotigotine (unconjugated + conjugated rotigotine) were slightly higher in subjects with mHI compared to HS. Median Cmax, ss and AUC (0-24, ss of total rotigotine were 38% and 14% higher in subjects with mHI compared to HS, respectively. Total clearance for total rotigotine was 24% lower in subjects with mHI compared to HS while renal clearance was similar in both groups. Urinary excretion of conjugated N-desalkyl metabolites was slightly higher in subjects with mHI compared to HS.

Conclusions: These data indicate that there is no accumulation of unconjugated rotigotine after repeated patch application in subjects with moderate impairment of hepatic function. No dose adjustment of rotigotine is needed in chronic treatment of patients with moderate impairment of hepatic function.

P2150
ACQUIRED HEPATOCEREBRAL DEGENERATION RESPONSIVE TO PENICILLAMINE: A CASE REPORT
G.A. Cocco1, S. Sotgiu2, K.S. Paulus3, V. Agenetti4, M. Conti5, G.P. Sechi7
1Istituto di Clinica Neurologica, 2Istituto di Scienze Radiologiche, Sassari, Italy

A 37-year-old man, affected by an HCV related liver cirrhosis, was admitted to our ward for a hepatic coma. Treated with rifaximin, lactulose and branched-chain aminocids infusion, his arousal state went back to normal in about 12 hours, and the ammonia levels decreased from 176 to 94 micromol/L; Physical examination revealed a slightly asymmetrical extrapyramidal syndrome, agitation, irritability and anxiety. Slit lamp examination, ceruloplasmin, cupremia and cupruria were within the normal range values. MRI revealed showed signal intensity in basal ganglia bilaterally on T1-weighted images. Cerebrospinal fluid examinations revealed an increased level of manganese concentration. Dopaminergic drugs (levodopa and pramipexole) were of no benefit. A treatment with penicillamine 900 mg/day and triessifenidile 4 mg/day was started; in the following 5 days, psychiatric disturbances progressively disappeared whilst bradikinesia, anamia, scialorrhea and dysarthria diminished; inconstant distal rest tremor was still present, but confined in the right upper limb; also postural instability improved. In the following 9 months, we observed a further progressive improvement in the extrapyramidal symptomatology. Acquired hepatocerebral degeneration (AHD) is a chronic brain disorder, which typically presents with dysarthria, ataxia, tremor, involuntary movements and altered mental status, and is caused by liver dysfunction and long-standing portal-systemic shunting. The pathophysiology of this disorder is still unknown, but hyperammonemia and/or cerebral manganese overload may play a role. Medical treatment is often disappointing. The progressive improvement of our patient’s symptomatology must be referred, in our opinion, to the penicillamine chelating properties toward manganese. Penicillamine can be a useful treatment for AHD.
P2151

MOVEMENT DISORDERS AND ADL IN HEAD-INJURED PATIENTS

F. Colonna

Rehabilitation Hospital, Fondazione San Raffaele, Ceglie Messapica, Italy

Literature testifies as the outcome of severe cranial trauma the appearance of involuntary movements arising from multiple subcortical haemorrhagic centres of infection or injuries of the rubro-cerebellar connections and of the superior cerebellar peduncle. The objective of this study is to evaluate and quantify involuntary movements and disabilities in a group of 12 subjects affected by outcome of serious head injury and presence of involuntary movements disturbing the rehabilitation process. The patients were first evaluated from time 0 to time 30 days; upon administration of a second-generation antiepileptic drug, levetiracetam, it was then evaluated after 3 and 6 months. Patients took levetiracetam in doses of 2000 mg/day. Measurements were effected by AIMS and GARS. The analysis of the results highlighted an AIMS statistical significance of p<0.005 after 3-months and of p<0.002 after 6 months. Regarding GARS, a statistical significance of p<0.003 after 3 months and of p<0.05 after 6 months was highlighted. These results show that:

- patients tolerated the administration of the drug well
- patients had a reduction in the single measurements carried out
- genuine reduction in spontaneous movements at 3 months with a p<0.005 associated with a reduction in ADL disability with a p<0.003
- this result is confirmed at the 6-month follow-up, with a p<0.002 for involuntary movements and a p<0.05 for disability in ADL
- patients at the 6-month follow-up did not show critical episodes and followed a monotherapy based on levetiracetam with a possibility of 2000 mg/d.

P2152

ACUTE HEMIBALLIC MOVEMENT SECONDARY TO CORTICAL INFARCTION

A. Constantinescu¹, C.D. Paposcu¹, O. Jerca¹, V. Constantinescu¹
1Department of Neurology, Rehabilitation Hospital, ‘University of Medicine and Pharmacy, Iasi, Romania

Background: Focal dystonia is classically considered a pure movement disorder of the basal ganglia, particulary the thalamus and striatum. We describe a case of focal dystonia following infarction of the fronto-parietal cortex.

Method: Case report of a 64-year-old woman with a history of hypertension and diabetes mellitus with a sudden onset of a severe right hand and lower leg involuntary movement of hemiballistic aspect. The neurological evolution was followed up for 6 months of motor rehabilitation.

Results: Computed tomography of the brain revealed lesions of infarction in the left fronto-parietal cortex. The hemiballistic movement decreased in severity and became ballism-chorea with a significant better outcome.

Conclusion: The pathophysiology of acute ballism-chorea in vascular lesion implies the cerebral cortex via cortico-striato-pallido-thalamo-cortical motor loops.

P2153

PRIMARY WRITING TREMOR AS AN EXAMPLE OF TASK SPECIFIC TREMOR – A CASE REPORT

S. Budrewicz¹, M. Dubik-Jerzierszka¹, M. Koszewicz¹,
K. Slotwinski, R. Podemski
1Department of Neurology, Medical University of Wroclaw, Poland

Primary writing tremor is a rare movement disorder appearing during writing, usually unilateral and progressive. The frequency of tremor is from 4.1 to 7.3 Hz. The pathogenesis is not clear and might be connected with peripheral disturbances or cortical and cerebellar lesions, similar to focal dystonia or essential tremor. The authors present the case of a 60-year-old, right-handed woman, working as an accountant, with right hand tremor. The disease lasted for 3 years. It appeared only during hand-writing, neither during other precise actions. It prevented her from working. She was forced to change her signature in the bank. Amantidine was administered in doses of 300 mg per day with very good effect. The tremor disappeared completely. The improvement has kept for one year. The authors indicated the great importance of the task specific tremor on the patients quality of life, mainly connected with professional work and the good results of adequate treatment.

P2154

LOAD-INSENSITIVE POSTURAL TREMOR IN CEREBELLAR ATAXIA ASSOCIATED WITH ANTI-GAD ANTIBODIES AND EVIDENCE OF CEREBELLAR GLUTAMATERGIC INVOLVEMENT WITH MR SPECTROSCOPY

G. Grimaldi¹, P. Jissendi², M. Manto¹
¹Department of Neurology, AUOP, Palermo, Italy, ²Department of Neuroradiology, ULB Erasme, ³Department of Neurology, ULB Erasme, Bruxelles, Belgium

Postural physiological tremor is characterized by a frequency ranging from 8 to 12 Hz, shifting towards lower values with load. Recent experimental studies indicate that a neurotoxicity associated with increased glutamate in cerebellar nuclei could be involved in the pathogenesis of cerebellar ataxia associated with anti-glutamic acid decarboxylase antibodies (anti-GAD-Ab). We analyzed postural tremor in a 16-year-old boy exhibiting ataxia associated with anti-GAD-Ab. The patient presented a bilateral down-beat nystagmus and ocular fixation instability. Laboratory examination showed positive anti-GAD-Ab (titer: 6.7%; N<2.6%). Brain Proton-MR-Spectroscopy (MRS) revealed some metabolic disturbances in cerebellar nuclei. In the cerebellum, total Glutamine&Glutamate/Cr was slightly increased (z score=2.02), supporting the hypothesis of glutamatergic pathways alternations by anti-GAD-Ab. We analysed postural tremor of the hand before and after mass addition (418 gr). Basal peak frequency was 8.13 Hz, with a low frequency component ranging from 0.87 to 5.12 Hz. With inertia, peak frequency was 9.5 Hz. Crest factor was 0.121 in basal and 0.125 (with mass). For the low frequency band, peak frequencies were 1.88 and 2.34 Hz respectively. Spectral analysis confirmed the insensitiveness to inertia (mean of peak intensities: 0.0041±0.00303 and 0.0034±0.001 without and with mass; p=0.706). Tremor studies in these patients are rare. We describe the first case of postural tremor insensitive to inertia in a young patient with anti-GAD-Ab. Anti-GAD-Ab generate a postural tremor distinct from physiological tremor, rendering oscillations refractory to inertia probably due to cerebellar damage. Our MRS findings seem to confirm the role of glutamate in the pathogenesis of cerebellar deficits.
P2155
GENETIC ASSOCIATION STUDY OF ESSENTIAL TREMOR IN A RUSSIAN POPULATION
S.A. Illarioshkin1, A.V. Karabanov, S.A. Klyushnikov, G.K. Bagieva, E.N. Tarasova, E.D. Markova, I.A. Ivanova-Smolenskaya
Department of Neurogenetics, Institute of Neurology RAMS, Moscow, Russia

Objective: To estimate the frequency and possible association with essential tremor (ET) of polymorphic alleles of some candidate genes in Russian familial and sporadic cases of ET.

Background: ET is one of the most common movement disorders affecting up to 4–5% in the general population. The genetic basis of ET is still unclear. Recently the segregation of some genetic polymorphisms (Ser9Gly variant in the DRD3 gene on chromosome 3q and 828C>G polymorphism in the HS1-BP3 gene on chromosome 2p) with ET has been found in some French and American families. The important goal now is to determine the possible significance of these polymorphisms in ET.

Methods: The group of ET patients was recruited for our study using criteria established by the Tremor Investigation Group. We examined 84 Russian patients (probands with familial ET (mean age 62.4±13.2), and 92 patients with sporadic ET (mean age 58.3±11.4). The control group consisted of 159 non-affected individuals (mean age 60.5±14.3). The molecular screening for the Ser9Gly and 828C>G polymorphisms was performed using the MscI and BseYI restriction assays, correspondingly.

Results: We found no statistically significant differences in Ser9Gly allele frequencies between familial, sporadic cases of ET and controls in our study. Interesting preliminary results on the 828C>G polymorphism in the HS1-BP3 gene in our cohort will be assessed for significance in our further analysis, and will be discussed in details later.

Conclusions: We performed the first genetic association study of ET in a Russian population.

P2156
DYSTONIA AS A CLINICAL MANIFESTATION OF ISCHEMIC LESIONS OF THE BASAL GANGLIA
N.S. Ivanovic, M.R. Svetel, J.J. Jovic, V.S. Kostic
Special Hospital for Cerebrovascular Disease, Institute for Neurology, Clinical Centre Serbia, Belgrade, Department for Neurology, Medical Centre, Sombor, Serbia

Introduction: Symptomatic dystonia can be caused by a different degenerative, metabolic disease, using the specific drugs and exposing to toxins. However, symptomatic dystonia is mostly the consequence of structural lesions, caused by cerebrovascular disease.

Objective and methods: Our investigation involved patients with symptomatic dystonias induced by cerebrovascular insults, in which we tried on basis of different types of clinical investigations and neuroimaging studies (CT/MRI) to define their clinical, demographic and pathomorphological characteristics.

Results: In a group of 33 patients (F:15/M:18), average age at the beginning of the disease was 56.5 years (range 35–75). Generalized dystonia had 6 of them, hemidystonia 10, segmental 3, torticollis 2, dystonia of the arms 3, blepharospasm 3, spasmocodic dystonia 1 and oromandibular dystonia 2. Hemidystonia was a statically significantly presenting feature disease induced by cerebrovascular disease (X2c=15.34, X2 0.05=14.067, X2 0.01=18.475, DF=7). In 16 of 33 (48%) of our patients, dystonia was developed after a latency period average 1.2 years (range 1 month – 5 years).

In 10/33 (30%) dystonia was the first, and 7/33 (21%) the unique clinical manifestation of stroke. Focal or multifocal ischemic lesions of the basal ganglia had 30/33 of our patients (16 putamen, 6 nc.lentiformis, 5 nc.caudatus and 3 globus pallidus), thalamus 6/33 and brainstem 4/33 (not statically significant difference between localization of the lesions and distribution of dystonia).

Discussion: In the case when ischemic lesion is located in basal ganglia, thalamus and brainstem, we can expect dystonia development. This lesion produces disconnection or change of neural circuits activity, with desinhibition of thalamus and thalamocortical projections.

P2157
RESTLESS LEGS SYNDROME AND INSOMNIA IN SHIFT WORKERS: A STUDY ON A GROUP OF NURSE PERSONNEL
K. Papadopoulos, E. Katsikandaraki, S. Stylianoudaki, I. Choustoulakis, A. Chamouzas
Neurological Clinic, Psychiatric Hospital of Tripolis, Greece

Background and aims: Evaluation of irregular shift-work effect on sleepiness and correlation with RLS in a population of nurse personnel in the Psychiatric Hospital of Tripolis.

Methods: A sample of 82 workers has been studied according to the criteria of the International RLS Study Group (RLS rating scale for severity) and Athens Insomnia Scale (AIS). The statistical analysis is based on t-criterion.

Results: 17.1% of the shift workers are positive for RLS. Mean RLS value is 13.4, which is considered low according to the 40 point scale. Both weight and gender do not affect significantly the accession of RLS (p=0.05). The disparity of RLS vs. non RLS patients arises significantly at the age of 41–50; longevity >20 years is also a significant factor (p=0.05). 92.9% of the shift-workers report insomnia symptoms (mean AIS score is 6.2±6 cut-off score) and especially difficulty in initiating sleep and early morning awakening.

Conclusions: RLS of low severity is common in the irregular shift-work nurse personnel. Longevity is a cumulative factor for RLS initiation and it must be further analyzed. Moreover, insomnia is a determinative symptom in the examined population.

P2158
PECULIARITIES OF VASCULAR PARKINSONISM IN PATIENTS WITH ACUTE STROKE (AS) AND TRANSIENT ISCHEMIC ATTACK (TIA)
T. Khamichenka, S.A. Likhachev
Department of Neurology, Hospital #5, RSPC of Neurology and Neurosurgery, Minsk, Belarus

Aim: The main reason of vascular parkinsonism (VP) development is atherosclerotic defeat of brain vessels that often is combined with arterial hypertension. The disease is mainly developed in persons older than 50, who have signs of chronic cerebral circulatory insufficiency or stroke in anamnesis. The aim of this study was to investigate prevalence and peculiarities of VP development in patients with AS and TIA.

Methods: 775 in-patients with AS and 156 with TIA were investigated. VP was observed in 8.38% (more often in male patients – 73.08%).

Results: In the anamnesis 93.59% patients had arterial hypertension, myocardial infarction was present in 15.38%; heart rhythm disturbance in 20.51%. 79.49% VP patients had ischemic infarction, 8.98% had hemorrhagic infarction, 11.54% – TIA. Repeated AS and TIA were observed in 37.18%. Pathologic process was more
often localized in the left cerebral hemisphere (53.85%). L-Dopa therapy was prescribed to 73.85% of patients. 45.24% had no effect from L-Dopa therapy, 54.76% had insignificant effect. Clinically VP was pictured by akinetic-corticig syndrome, only 2.56% had a tremor of arms. CT and MRI revealed vascular foci in the basal nucleus in 29.49%. Cognitive dysfunctions were found in 38.47%, hemiparesis in 80.77%, coordinative disorders in 23.08%, oculomotorius in 8.97%, bulbar-pseudobulbar in 14.11%, aphasia in 28.01%

Conclusion: Thus, VP in AS and TIA patients is characterized by predominance of akinetic and rigid forms, insignificant effect of L-Dopa therapy, vascular foci in basal nuclei, signs of lesion in another brain structures.

P2159
PREGNANCY AND PARKINSON’S DISEASE
L. Khatiaishvili1, K. Akhvlediani2, M. Kapiandize1
1Department of Neurology, Tbilisi State Medical University, Tbilisi, Georgia
2Research-Practical Center for Control and Prevention of Epilepsy, Tbilisi, Georgia

Neurologists do not have many opportunities to observe the natural history of Parkinson’s disease (PD) during pregnancy at least because the majority of women with PD are not in a childbearing age. There are only several case reports in literature and most of them state that the condition of women with PD during pregnancy and/or afterwards gets worse. We observed a 39-year-old woman who had PD since she was 35. Disease started with hemiparkinsonism and involved axial and contralateral muscles within the first year of sickness. At the age of 36 she had rest tremor in both hands, prominent hypokinesia and rigidity in extremities and axial muscles. She had no Kaizer-Flasher ring, her ceruloplasmine was normal. Brain MRI did not reveal any abnormalities. She started to receive piribedil 150 mg/day with positive effect, then levodopa/benserazide 750mg/day with positive effect, but after several months she began to experience the wearing off phenomena. She became depressed and gave up all the medications. That resulted in significant worsening of her symptoms. Than she became pregnant. During pregnancy the symptoms started to improve gradually. In the 30th week of pregnancy she had only minimal rest tremor in one hand, slight hypokinesia, almost no rigidity. She gave birth to a healthy boy through Caesarean section. This case may illustrate the positive effect of female sex hormones on PD symptoms, and this issue needs further inquiry.

P2160
UROLOGIC DYSFUNCTION IN PARKINSON’S DISEASE (PD)
E. Khitarishvili1, N. Fyodorova2, M. Aloeva1
1P. Sarajishvili Institute of Neurology and Neurosurgery, Tbilisi, Georgia, 2Department of Neurology, Russian Medical Academy, Russia

The aim of our study was to investigate character and clinical features of urination disorders between clinical signs of disease and types of urologic dysfunction, as well as to estimate the effectiveness of urologic disturbances medical treatment. The degree of PD severity was evaluated by beans of Hoehn and Yahr scale, UPDRS, affective disorders – Hamilton depression and Taylor anxiety scales, the quality of life indices – ADL scale, PDQ-39, QOL, vegetative disorders – Korshunov, Levin scale. We studied 75 PD patients. The degree of PD severity by Hoehn and Yahr – 2.9±0.4 score. The duration of urologic dysfunction in PD patients was 2.1±1.1 years. The bladder hyperactive syndrome was diagnosed in all patients. Clinical features are expressed by frequent, urgent urination with associated with urgent urinary incontinence in all except one. The distinct correlation was determined between the onset of urination disorders, PD clinical forms, as well as the degree of urination disorders and worsening of the quality of life indices. The treatment of the bladder hyperactive syndrome included dose correction of antiparkinsonian drugs, training the bladder and urogenital diaphragm muscles by Kegell and medical treatment with M-cholinoblockers. We conclude that complex symptomatic therapy of urologic dysfunction in PD patients by low doses of cholinoblockers will decrease the signs of bladder hyperactivity and significantly improve the quality of life.

P2161
A CASE OF ADULT-ONSET HUNTINGTON’S DISEASE PRESENTING WITH ATYPICAL IMAGING FINDINGS
O. Koutoula, K. Papadopoulos, A. Boutsis, N. Taskos
Neurologic Department B’, AHEPA University Hospital, Thessaloniki, Greece

Introduction: Huntington’s disease (HD) is a lethal autosomic dominant degenerative disease resulting from an expansion of a CAG repeat within the IT15 gene on chromosome 4p16.3. The striatum is known to be the principal affected structure in HD patients. However, there is evidence that atrophy is widespread and that subcortical atrophy might be associated with cortical changes. We report an adult-onset case of Huntington disease with atypical neuroimaging findings.

Case report: The patient, a 45-year-old woman, was admitted to our clinic because of progressive involuntary movements. Her father and grandfather suffered from the similar symptoms. Neurologically, she had subcortical dementia, generalized chorea and spasticity. MRI demonstrated grey matter atrophy particularly of parietal lobes without remarkable increase of the bicaudate ratio. However, DNA analysis showed CAG expanded repeats in the Huntington gene (45/24).

Discussion: Many studies have used volumetric analysis to demonstrate progressive bilateral atrophy of the striatum, which may occur gradually even years before motor symptoms appear. Recent evidence from neuroimaging studies suggests that the neurodegenerative changes in HD extend to cortical grey matter and cerebral white-matter regions. However, it remains unknown whether the cortical degeneration is a primary or a secondary feature of the HD degenerative process, or both. The point is that cortical atrophy is now admitted as an earlier and more widespread characteristic of HD than previously expected.

P2162
FATIGUE-INDUCED HIGH-FREQUENCY TREMOR COMPONENTS DETECTED BY A WEARABLE TREMOR COHERENCE ANALYZER
F. Brunetti1, M. Manto1, J.L. Pons1
1Bioengineering Group, Instituto de Automática Industrial, CSIC, Madrid, Spain, 2Laboratory of Experimental Neurology, Université Libre de Bruxelles, Hôpital Erasme, Bruxelles, Belgium

Coherence has been used in neurology to track periodic signals. The Tremor Coherence Analyzer (TCA) is a portable tool to assess tremor in real time, calculating instantaneous coherence between two channels. Besides transmitting raw data to a computer, the TCA can track tremor oscillators. Studies on coherence have shown the use of the coherence to detect sudden oscillators in subjects with ET, PD and Dyskinesia. Physiology of tremor pathologies has also been described using coherence analysis. We carried

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
out a fatigue study in 3 healthy subjects (M39, M28 and M27). The analyzed set included “outstretched arm” (T1) and “finger to nose” (T2) tasks. Tasks were 1 minute long and every subject repeated it 5 times. In order to induce tremor, subjects held a 1 kg mass during tasks. Two sEMG sensors were placed on Biceps and Triceps of the same limb. In T1, spectral analysis has shown primary peaks of fatigue-induced tremor in 14-16 Hz band and secondary peaks in 8-12 Hz band. The power in these bands increased with time. The voluntary component was visible in T2 data remarking the need for protocols for kinetic tremors. In T2, the tremor activity (10-15 Hz) was flatter than in T1 due to the variability of movement repetitions. The coherence analysis revealed high cross-talk effect between biceps and triceps sEMG signals. This result was expected due to the proximity of the involved muscles. We show that the behaviour of oscillators can be unravelled immediately with a wearable coherence analyzer in fatigueing tasks.

**P2163**

**THE MODULATION OF HIGH FREQUENCY OSCILLATIONS DURING ADAPTATION TO INERTIA**

G. Grimaldi1, M. Manto2

1Department of Neurology, AUOP, Palermo, Italy, 2Departement de Neurologie, FNRS ULB, Bruxelles, Belgium

**Background:** Physiological tremor of the hands is characterized by a frequency ranging from 8 to 12 Hz, shifting towards lower values when a mass is added. High frequencies in the range of 20–30 Hz are considered to be indicative of the central commands.

**Objective:** To study the contribution of different frequency bands in hand tremor during the inertial test. To assess whether different groups of neurological patients present distinct responses in different frequency bands.

**Methods:** We recorded postural tremor of the hand without and with added mass (418 gr) in 17 patients (essential tremor (n=7), cerebellar disease (n=5), Parkinson’s disease (n=1), Lewy Body disease (n=1), monoclonal gammopathy (n=1),iatrogenic tremor (n=1), post-traumatic movement disorder (n=1); mean age: 59.14±22.5; F/M:11/6. Spectral analysis of the tremor was evaluated using FFT (epochs of 5 sec; 512 Hz). Peak frequencies, integrals of 2–5, 2–20 and 20–30 Hz bands were computed.

**Results:** We identified 2 groups of patients. Group 1 showed an increase with mass both in the 2–5 and the 2–20 Hz bands (127±18% and 135±29% respectively), as compared to the 20–30 reference band. By contrast, Group 2 showed a decrease both in the 2-5 and 2-20 Hz bands (60±12% and 63±9% respectively), as compared to the reference band. However, the mean basal frequencies were similar in both groups (6.10±2.27 and 4.18±1.69 Hz; t test: p=0.107).

**Conclusion:** We observed distinct motor behaviours in our patients. Our results are in agreement with the hypothesis of hyper-adaptation of motor cortex in a subgroup of neurological patients.

**P2164**

**FALLS IN DIFFERENT TYPES OF PARKINSON’S DISEASE**

M. Marona, M. Rudzińska, S. Bukowczan, K. Banaszkiewicz, A. Szczudlik

Department of Neurology, Jagiellonian University Medical College, Krakow, Poland

**Background:** Falls are more common in Parkinson’s disease (PD) patients than in an elderly population, but their causes are not well recognized.

Aim: To assess the frequency and causes of falls in Postural Instability and Gait Difficulty (PIGD) versus tremor type PD patients in the retrospective study.

**Material and methods:** 106 moderately advanced PD patients (mean disease duration: 6.3±3.5 years) were asked about the numbers and circumstances of falls in the previous year. Causes of falls were classified according to Olanow. The types of PD were defined according to Jancovic criteria.

**Results:** There were 76 patients with PIGD and 21 with tremor type. Patients in both groups did not differ regarding to: gender, age, disease duration, age of disease onset, UPDRS-score, Schwab & England and mental status. Patients with PIGD vs. tremor type had significantly more often dyskinesia, fluctuation and freezing. Falls were significantly more common in PIGD-PD (58%) than in tremor type (24%) (p<0.005). Number of falls in PIGD-PD patients was significantly higher than in tremor type (3.6±6.0 vs. 0.6±1.8, p<0.005, respectively). Main cause of falls in both groups were sudden falls and environmental factors. Freezing, orthostatic hypotension and coexisting neurological disease were reasons of falls only in the PIGD type.

**Conclusions:** PIGD-PD patients are significantly more predisposed to falls. Sudden falls are the most frequent cause of falls in both types of PD.

**P2165**

**MOTOR, AFFECTIVE AND COGNITIVE DYSFUNCTIONS CORRELATE IN ADVANCED PARKINSON’S DISEASE**

I.V. Litvinenko, V.I. Mogilnaya, O.S. Sologub

1Department of Neurology, Medical Military Academy, St. Petersburg, Russia

Freezing of gait (FOG), postural instability and gait difficulty (PIGD) are disabling phenomena common in patients with advanced Parkinson’s disease (PD). The cause of these is unclear. The objective of this study was to explore a hypothesis stating that FOG and PIGD are related to cognitive decline and affective disorders.

**Materials and methods:** 62 PD patients who fulfilled UK Brain Bank criteria for PD (41 – non demented PD group, 20 – demented PD group with onset of dementia at least two years after parkinsonism) participated in this study. Motor, cognitive, psychiatric symptoms were assessed using clinical assessment as well as rating scales including the Hoehn&Yahr stage, the Unified Parkinson’s disease Rating Scale (UPDRS), the Mini-Mental State Examination (MMSE), clock drawing test (CDT), Frontal Assessment Battery (FAB) and the Neuropsychiatric Inventory (NPI-12) «serial 7s subtraction» task from MMSE were chosen as a measure of attentional control and working memory. Statistical analysis was tested using multiple regression and Spearman correlation analysis.

**Results:** Worse performances on tests of attention «serial 7s subtraction», spatial and visual construction (CDT) and executive functions (FAB) correlated with measures of FOG and PIGD (points 14, 15, 29, 30 in the UPDRS). Anxiety, apathy NPI items correlated with FOG (r=0.32 and r=0.29, p<0.05).

**Conclusions:** These findings raise the question whether PIGD and dementia share a common neuropathology and non-dopaminergic neurotransmitter origin. Therapy in advanced PD should include compounds improving attention, executive functions and decreasing affective symptoms.
P2166
DESIGN OF A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF PRAMIPEXOLE IN RLS PATIENTS WITH ASSOCIATED MOOD DISTURBANCE
P. Montagna1, J. Koester2, G. Crespi1
1Department of Neurological Sciences, University of Bologna, Italy, 2Medical Division, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

Purpose: Mood disturbance is common in restless legs syndrome (RLS). Insomnia is also common, and may contribute to mood disturbance. Recent studies suggest that in RLS, the dopamine agonist pramipexole may have antidepressive effects. To test the treatment in RLS patients with mood disturbance, we have initiated a double-blind, placebo-controlled 12-week trial.

Methods: Across 9 European countries, 360 patients will receive pramipexole or placebo. Patients will meet all criteria of the International RLS Study Group, with a score >15 on the group's rating scale (IRLS), RLS symptoms ≥2 days weekly for the preceding 3 months, and at least moderate mood disturbance (a score of ≥2 on IRLS item 10). During the first 4 weeks, pramipexole will be flexibly uptitrated to 0.125, 0.25, 0.5, or 0.75 mg/d.

Endpoints: The trial’s primary endpoints will include 12-week change in IRLS total score, and also patients’ outcome on the Beck Depression Inventory (BDI-II). Secondary endpoints will include responder rates on IRLS, BDI-II, and the Clinical Global Impressions scales. Other endpoints will assess anxiety (Hospital Anxiety and Depression Scale–Anxiety subscale), sleep quality (RLS-6), limb pain (visual analogue scales), quality of life (Johns Hopkins RLS-QOL), and adverse events.

Conclusions: The trial has the potential to demonstrate the efficacy and safety of pramipexole for RLS patients with concomitant mood disturbance. In addition, this is the first trial using structured instruments to assess pramipexole’s benefit for affective RLS symptoms.

Disclosure: Dr Montagna was involved in trials with GlaxoSmithKline, Boehringer-Ingeheim and Schwarz Pharma and received consultant honoraria from Boehringer-Ingeheim.

P2167
SLOW-ONSET TASK-SPECIFIC LIMB DYSTONIA: AN INITIAL SYMPTOM OF PARKINSON’S DISEASE OR ASSOCIATION OF TWO DISORDERS?
I. Nestrasil, P. Kanovsky
Department of Neurology, Palacky University, University Hospital, Olomouc, Czech Republic

Objectives: We describe two cases of sporadic occurrence of task-specific limb dystonia (writer’s cramp) with slow onset and with subsequent development of parkinsonian symptoms.

Methods: Two men suffered from task-specific dystonia and subsequently mild parkinsonian symptoms (Hoehn&Yahr 1.0) developed. A 46-year-old man (patient A) was referred for a graphospasm, which occurred 3 years before. After 2 years of disease course, a positionally-sensitive tremor occurred and some months later he started complaining of right hand stiffness. A 59-year-old man (patient B) complained of writer’s cramp. It had appeared 6 years ago and did not progress. Later he noticed a hypokinesia and resting tremor of his right hand. MRI of the brain and C spine were normal in both subjects.

Results: Neurological examination showed a dystonic pattern typical for graphospasm in both subjects during writing with the right hand. In both subjects there were hypomimia, mild hypokinesia and rigidity, and decreased arm swinging of the right upper limb. In patient B there was also resting tremor of the right hand. L-dopa significantly alleviated parkinsonian symptoms. Polymyography showed a dystonic pattern with muscle hyperactivity of wrist flexors.

Conclusion: Task-specific limb dystonia preceding a development of Parkinson’s disease is a very uncommon condition. It remains unknown, whether writer’s cramp can precede the development of Parkinson’s disease or whether these cases present an association of two different disorders. The present work shows that a pathophysiology of both writer’s cramp and Parkinson’s disease can be related.

P2168
PSYCHOSIS DUE TO ERYTHROMYCIN IN A CABGEROLINE TREATED PD PATIENT
A. Oliveros Cid1, A. Oliveros Juste2, M.A. Cid Lopez2, F. Mora5, I. Perez Lopez-Fraile1, N. Fayéd6
1Servicio de Neurología, Clinica Quiron Zaragoza, 2Servicio de Neurología, Policlinica Sagasta, 3Servicio de Neurofisiología, 4Servicio de Medicina Interna, Clinica Quiron Zaragoza, 5Servicio de Neurología, Hospital Universitario Miguel Servet, 6Servicio de Neuroradiología, Clinica Quiron Zaragoza, Spain

Ergotic dopaminergic agonist can show clinically relevant interactions with different macrolides. Newer semisynthetic drugs seem to show less interaction, but erythromycin has shown to rise up to four times bromocriptine levels in healthy volunteers. The mechanism of this interaction seems to be related to citocrom P450 inactivation.

Patient: We present the case of an 81-year-old woman affected with Parkinson’s disease 7 years before. She was taking Cabergoline (6 mg/day), L-dopa (800 mg/day), halazepam (20 mg/day) and amiodipine. She was admitted because a history suggested of a pneumonic process, initiating treatment with erythromycin (1500 mg/day) and paracetamol (acetaminophen). 6 years after initiating antibiotic therapy she developed an episode of hallucinations, confusion, temporal-spatial disorientation, agitation and choreic dyskinesias.

Results: A CT-Scan was performed, to discard acute brain damage. Blood test was normal, except for increase of leucocytes (neutrophils) and VSG. Temperature was 37.4˚C. After initial evaluation, we decided to decrease cabergoline treatment to 2 mg/day and L-dopa to 600 mg/day, with progressive reduction of psychotic symptoms. UPDRS motor subscore showed almost no change in spite of reduction of L-dopa and, specially, cabergoline. After finishing erythromycin treatment, cabergoline and L-dopa were given again at previous dosage.

Conclusion: Macrolides, especially “classic” ones, should be used carefully in patients under treatment with antiparkinsonian ergotic derivatives. Particularly, erythromycin should be avoided, and if needed, ergotic treatment should be reduced. So far, this is the first description we found of a significant interaction between erythromycin and cabergoline in a parkinsonian patient.

P2169
NEUROACANTHOCYTOSIS AND EPILEPSY: A CASE REPORT
K. Papadopoulos1, O. Koutoula, G. Kontogounis, N. Taskos
Department of Neurology B, Aristotle University of Thessaloniki, Ahepa University Hospital, Thessaloniki, Greece

Background: Neuroacanthocytosis, is a rare neurodegenerative disorder, with genetic heterogeneity. It can be autosomal dominant, recessive or even sporadic. It is caused by mutations in VPS13A,
which encode a large protein called chorein (chromosome 9q21).2. The erythrocytes have an appearance characterized by irregular spines arising from the cell surface, (acanthocytes). In affected patients, acanthocytes account for at least 10% of all peripheral red blood cells. Its clinical manifestations are variable, including involuntary movements, cognitive and behavioural changes, orofacial dyskinesia, seizures and peripheral neuropathy.

Methods: We report a case of neuroacanthocytosis, in which the presenting symptom was epileptic seizures for 10 years without any other cardinal manifestation. The patient is a 50-year-old female, whose main manifestation was simple partial seizures treated with antiepileptics. 10 years later on, chorea of the right upper limb emerged, along with decline of cognitive function, extrapyramidal dystonic posture, hyporeflexia and apathy.

Results: Diagnosis was suggested on a clinical basis and confirmed by identification of acanthocytes in the peripheral blood smear (>39%). Magnetic resonance imaging performed was normal, neurophysiologic testing was normal, creatine kinase (CK) was 754 mg/dl. Mini mental state examination valued 10 in scale of 30. The clinical course remained stable, after one year follow-up.

Conclusions: Neuroacanthocytosis is a rare condition with miscellaneous symptoms and signs. Some of its core features are shared by other diseases. Therefore it has to be differentiated from them. It is thus important to suspect neuroacanthocytosis and perform the blood testing even when the initial presentation is atypical.

P2170
ANALYSIS OF SYMPTOM-PREDICTORS IN THE DEVELOPMENT OF PARKINSON’S DISEASE
I. Petrov
Movement Disorders Department, Clinic of Neurology, Clinical Center, Skopje, Macedonia

Aim: To present symptoms-predictors for possible further development of Parkinson’s disease.

Background: The patients in their pre-symptomatic phase had the following symptoms: inversion of sleep–excessive daytime sleepiness and insomnia by night, hiposmia, anosmia, difficulties in recognition of odours, constipation, diarrhea, obesity, prolonged QT interval on the electrocardiogram (EKG) and Restless legs syndrome. These symptoms were predictors in further development of PD.

Material and methods: 120 patients were investigated over a period of 5 years at the Movement Disorders Department, Neurology Clinic in Skopje. 70 of them were men and 50 women, at age 44–73 all suffering from PD. In patients at age from 44–53 dominant symptoms were obesity, anosmia, hiposmia and restless legs syndrome (RLS). In group 54–63 years of age difficulties in recognition of odours, constipation, diarrhea and RLS. In the last group 64–73 years, inversion of sleep and prolonged QT interval were dominant.

Results: We found inversion of sleep in 80 patients, anosmia in 10, hiposmia in 50, difficulties in recognition of odours in 70 patients, constipation in 100, diarrhea in 50, RLS in 50, obesity in 40 and prolonged QT interval in 60 of the patients.

Discussion: The analyzed symptoms are important in pre-PD state and serve as a predictor for further development of PD and recommendation of the patients for frequent controls with the purpose of early diagnosis and quick initial treatment of PD with the aim of slowing the evolution of this chronic disease.

Conclusion: The analysis of the symptoms is important by aiming to pay more attention to pre-PD state of these symptoms predictors, because of their involvement in a high percentage of patients with PD.

P2171
PDQ 39 CORRELATES WITH “ON” TIME IN PATIENT DIARIES IN FLUCTUATING PARKINSON’S DISEASE PATIENTS
B.O. Popescu1, O. Bajenaru1, D. Obretin1, D.F. Muresanu2
1Department of Neurology, University Hospital Bucharest, Bucharest, Romania
2Department of Neurology, ‘Iuliu Hatieganu’ University, Cluj-Napoca, Romania

Background and aims: Advanced Parkinson’s disease (PD) still requires evaluation scales to be used in regular patient visits and in clinical studies. Recently developed PDQ 39 scale is not fully related to other scales used in PD, and quality of life is one of the main targets of the PD therapies nowadays. Therefore, in this study, we decided to explore the statistical correlation between the PDQ 39 questionnaire results and ‘on’ time results from the patient’s diaries.

Methods: We defined as main inclusion criteria idiopathic PD with motor fluctuations. Exclusion criteria were any other serious diseases that could alter quality of life.

Results: In our analyzed pool of patients, age was between 44 and 70, PD was diagnosed from 2 to 17 years before inclusion, motor fluctuations started from 0.08 to 8 years before inclusion, and dyskinesias were present in 7 of 11 patients. UPDRS ‘off’ scores were between 44 and 106, Schwab and England ratings were between 50% and 80% in ‘off’ and Hoehn and Yahr staging was between 2 and 4 in ‘off’ state. We found that PDQ 39 scores seem to correlate with on-time in patient diaries (r=0.61, p=0.09), and inversely correlate with off-time in diaries and Schwab and England rating. No correlation tendency was noted between PDQ 39 score and age of the patient, duration from disease onset, and presence of dyskinesia.

Conclusions: PDQ 39 seems to be an easy-to-estimate and well-correlated index with other capital evaluation scales in PD.

P2172
L-DOPA-INDUCED DYSKINESIA IN PARKINSON’S DISEASE: THE FRENCH DopamiP SURVEY
O. Rascol, L. Negre-Pages, DoPaMiP Study Group
Departments of Clinical Pharmacology and Neurosciences, Toulouse Medical School, Toulouse, France

The prevalence and clinical features of patients with L-dopa-induced dyskinesia (LDID) remains debated. We studied LDID in a large series of ambulatory patients with Parkinson’s disease (PD) recruited in 28 non-specialized neurological out-patient clinics. We studied 419 PD patients (mean age = 69±9 years, mean disease duration = 6±4 years, HY median score=2) using UPDRS and self-questionnaires assessing anxiety/depression symptoms (HADS-A>7: 60% vs. 44%, p<10-4) and anxious symptoms (HADS-D>7: 56% vs. 32%, p<10-4; 39±19 vs. 31±16, p<10-4). LDID patients had more depressive and anxious symptoms (HADS-D>7: 56% vs. 32%, p<10-4; HADS-A>7: 60% vs. 44%, p<10-4) and poorer QoL (35 ±13 vs. 24±13, p< 10-4). LDID patients had longer treatment duration (8±5 vs. 4±3, p<10-4), and received higher L-Dopa equivalent daily dose (1424 ±959 vs. 793±669, p<10-4).
P2173

DEPRESSION AND PSEUDO-DEPRESSION IN PARKINSON’S DISEASE

D. Reisz1, M.A. Simu1, D.R. Chirileanu2, S. Tamasan2
1Department of Neurology, University of Medicine and Pharmacy, 2Department of Psychiatry, County Hospital, Timisoara, Romania

The aim of this paper is to describe the depressive-like neuropsychiatric complaints in Parkinson’s disease patients. It is well known that depressive symptoms frequently occur in Parkinson’s disease populations and the prevalence rates have been reported from 11% to 44% depending upon the presence of minor or major depressive symptoms and the assessment scale used. We examine 48 idiopathic Parkinson’s disease patients and we note the age, the duration of disease, the stage of disease, score UPDRS, the drugs used, the co-morbidities. All the patients were cognitive intact (MMSE>26), and were questioned after an informed consent. The battery of tests used consisted of Beck Depression Inventory, HAM-D, HAM-A, Geriatric Depressive Scale and a list of 50 depressive-like and depressive items. We used a quality of life questionnaire.

Conclusions: The actual scale used for identifying depression tends to overstate the incidence of the depression in Parkinson’s disease because of an overlapping between symptoms of Parkinson’s disease and some symptoms of depressive disorder (flat affect, inability to work, fatigue, preoccupation with ill health, loss of desire, and reduction in libido). The emerged list with depression-like symptoms could be a list of those depressive aspects mediated by dopaminergic systems. The list affords us to characterise this particular group of patients and we could compare neuropsychiatric traits in Parkinson’s disease with similar data in Europe.

P2174

Abstract cancelled

P2175

IMPACT OF AN INTENSIVE “LOUD AND CLEAR” SPEECH THERAPY PROGRAM ON VOICE AND SPEECH IN A DYSARTHRIC INDIVIDUAL WITH PARKINSON’S DISEASE AND A DBS-STN IMPLANT

S. Sapir
Department of Communication Sciences and Disorders, University of Haifa, Israel

Background and aims: Dysarthria associated with idiopathic Parkinson’s disease (IPD) has not responded well to medication, brain surgery, deep brain stimulation (DBS), and traditional speech therapy. DBS-STN may worsen speech. The purpose of this study was to assess the impact of an intensive “loud and clear” speech therapy (LCST) program on voice and speech in a 59-year-old man with a 12-years history of Parkinson’s disease and one-year history of using DBS-STN.

Methods: The patient’s voice was recorded at the onset (PRE) and offset (POST) of the 1 month LCST program. Treatment and recordings were done with the DBS on. At both PRE and POST recording sessions, the patient’s voice was recorded during paragraph reading (“grandfather passage”, Hebrew translation) and free speech. Thirty (30) university students, graduates of a clinical training program in communication disorders, served as judges. They each independently rated the speech samples of the patient’s recordings at PRE and POST, using interactive software with a multidimensional 10 cm visual analogue scale (MD-VAS), and a crossover design.

Results: There was marked and significant improvement in the PRE to POST rating of the 4 dimensions of speech: voice quality, prosody, speech intelligibility, and overall speech quality. Patient’s and family members’ reports indicate that the therapeutic gains have been maintained as long as the latest follow-up call, 3 months post LCST.

Conclusions: Albeit preliminary, these findings suggest that the LCST may be an effective method in the treatment of parkinsonian dysarthric speech, with and without the DBS-STN.

P2176

A SLOW FLOW ARTERIO-VENOUS MALFORMATION (AVM) AS A CAUSE OF A NEURO-PSYCHIATRIC SYNDROME COMPRISING DYSTONIA AND BEHAVIOURAL CHANGES

M.A. Sierra-Beltrán1, U. Rodríguez-Ortiz2, M.S. Rodríguez y Rodríguez2
1Department of Internal Medicine, Médica Sur Hospital, 2Neurology and Neurosurgery National Institute, Mexico City, DF, Mexico

A 16-year-old male patient suffering a neuro-psychiatric syndrome, comprising hemi-dystonia and behavioural changes is presented. His current illness began in 1997 with right arm movements limitation. 3 years later right forearm and hand involuntary movements developed. He was right-handed; after 1997 he gradually became left-handed. In 2001 a paediatric neurologist examined him, who then requested image studies (CT cranial scan) that showed a hyperdense image at the left putamen, interpreted as a calcification. He was medicated with Haloperidol, later shifted to Propranolol both without a significant functional improvement. Since 2004, stereotyped right upper and lower limbs involuntary movements (coreo-a-thetosis) and intentional tremor appeared. His family noticed an attitude of social interaction avoidance. He was admitted to the Neurology and Neurosurgery National Institute (Mexico City) in May 2006, where imaging studies were requested, and MRI cranial scan. This revealed a left putaminal vascular maze and a dilated Rosenthal vein. Thus, an angiographic cranial vessels study was requested, that revealed a slow flow left putaminal AVM. A neuropsychiatric evaluation found a verbal memory and attention impairment with a social isolation tendency. Because of the finding of a hyperdense putaminal lesion, resembling a calcified lesion, it was considered that the case may have corresponded to an infrequent presentation of Fahr Syndrome. A detailed analysis of the MRI scan images lead to the finding of a basal ganglia AVM partially occluded, after a prior haematoma (later calcified) associated with a left thalamic angioma. Putamen is an AVM rare location.

P2177

CEREBROLYSIN IS NEUROPROTECTIVE AFTER PROTEASOMAL INHIBITION AND SERUM DEPRIVATION IN A SH-SY5Y NEUROBLASTOMA CELL LINE

R. Stoica1, S. Budui1, B.O. Popescu2
1Department of Neurology, University Hospital, ‘Carol Davila’ University of Medicine and Pharmacy, 2Victor Babes’ National Institute of Pathology, Bucharest, Romania

Parkinson’s disease (PD) is a multifactorial disease caused by both genetic and environmental factors. Oxidative stress and proteasomal dysfunction are deleterious factors that play important roles in the pathogenesis of PD, but their interactions are not yet clear. Using a neuroblastoma SH-SY5Y cell line, we tried to reproduce these insults in a phenotype of dopaminergic cells. We investigated the effects of treatment with Cerebrolysin (Cere), a
peptidergic drug with nerve growth factor-like activity, on cell survival. Cere was previously proved to be neuroprotective in in vitro models of brain ischemia. Proteasomal inhibition was achieved after 24 hours exposure to lactacystin (LC), in doses that significantly reduce proteasomal activity and induce significant apoptosis. Additionally, the cells were exposed to serum deprivation (SD) stress. In cell cultures, SD is linked with an increase in reactive oxygen species production that leads to apoptosis. The cellular viability was assessed by an MTT-reduction assay. The treatment with Cere resulted in a dose-dependent and significant rescue of neurons subjected to the double insult: proteasomal inhibition and SD. Cere also increased cellular viability after SD without LC treatment, but not after the LC treatment only. In conclusion, the results indicate that Cere has neuroprotective properties, possibly through a neurotrophic signal transduction-linked effect. Due to the complex composition of the drug, most likely different synergistic effects contribute to its protective properties. Next, we will investigate the alpha-synuclein expression in our cultures through immunoblotting and immunocytochemistry techniques to strengthen the implications of this cellular model for PD.

P2178
PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF SNT-MC17/IDEBENONE IN HEALTHY ADULT MEN
K. Kutza, P. Vankan
‘AccelPharm, Basel, ‘Santhera Pharmaceuticals, Liestal, Switzerland

Aims: Four single-centre, open-label studies were conducted (Studies I, II, III, IV) to determine pharmacokinetics (PK), effect of food on PK, and safety and tolerability of idebenone.

Methods: Subjects received either single doses of idebenone 150 mg, 750 mg, or 1050 mg (Studies I-III), or multiple doses at 150 mg tid or 750 mg tid for 14 days (Study IV).

Results: A total of 69 subjects enrolled (Study I, n=8; Study II, n=8; Study III, n=28; Study IV, n=25). There was high inter-subject variability in idebenone PK. Maximum plasma concentrations (Cmax) of unchanged idebenone increased dose-dependently, ranging from 1.64±0.99 ng/mL (150 mg dose) to 10.23±8.40 ng/mL (1050 mg dose). There was no accumulation of idebenone when dosed for 14 days at 750 mg tid. Time to Cmax (tmx) was 3.5h after a single dose, decreasing to 0.67h after repeated dosing. Bioavailability of pharmacologically active parent idebenone increased 4-fold following a fat-rich meal. Idebenone metabolites appeared in the plasma nearly synchronously with parent idebenone, indicating a high first-pass effect. Most idebenone (65%) was excreted in the urine as conjugated metabolites. A total of 4 types of AEs occurred during studies I, II, and III; in study IV, the most common AEs were chromaturia (n=6), headache (n=9), fatigue (n=9), and gastrointestinal disorders (n=11). There were no serious AEs and no clinically relevant changes in physical exams, vital signs, ECGs, or laboratory values in any study.

Conclusions: Idebenone exhibits linear PK over a range of 150–2250 mg/day, and is generally safe and well tolerated in healthy adult men.

P2179
COGNITIVE DECLINE AS A PREDICTOR OF THE PROGRESSION OF PARKINSON’S DISEASE
E.V. Vostrikova, P.I. Pilipenko, V.V. Vardasanidze, T.V. Voroncova
‘Department of Clinical Neurology, Novosibirsk State Medical University, ‘Novosibirsk Center of Extrapyramidal Diseases, ‘Regional Hospital of War Veterans, Novosibirsk, Russia

Background: Recent studies suggest that patients with Parkinson’s disease have a 5-6-fold greater risk of developing clinically significant cognitive decline over the course of the disease. Elderly subjects with mild parkinsonian signs but without Parkinson’s disease or dementia had a higher risk of developing dementia than those without parkinsonian signs. The aim of our study was to investigate the level of cognitive impairment at the different stages of Parkinson’s disease. Research problems were to determine risk factors of cognitive decline in this group of patients, investigate the influence of the level of cognitive impairment on progression of Parkinson’s disease.

Materials and methods: 50 patients with idiopathic Parkinson’s disease (12 males, 38 females, mean age 66.08±3.12 years, mean duration of Parkinson’s disease 9.9±1.64 years, mean duration of cognitive decline 3.43±1.05 years) and 40 age-matched healthy controls. We analyzed symptom history, results of clinical examination; neuropsychological and laboratory testing.

Results: Cognitive impairment was observed at the different stages of Parkinson’s disease; relationship between extrapyramidal and cognitive disturbances was revealed (correlation of total score of Mini Mental State Examination and stage of the disease was strong, r2=0.05); besides that, most of the patients had depression and it was more clinically severe in patients with rapid progression of Parkinson’s disease; some of them had depression before the onset of the main typical features of Parkinson’s disease.

Conclusions: Cognitive impairment and depression are predictors of disease progression.

P2180
MOOD EVALUATION IN THREE DOUBLE-BLIND TRIALS OF PRAMIPEXOLE FOR RESTLESS LEGS SYNDROME
J.W. Winkelman, J. Koester
‘Division of Sleep Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA, ‘Medical Division, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

Background: Mood disturbance is common in restless legs syndrome (RLS) and may represent dopaminergic dysfunction. It is unknown whether dopaminergic therapy for RLS can affect mood.

Methods: Trials of 3 and 12 weeks studied pramipexole at fixed doses of 0.125 or 0.25 to 0.75 mg/d. A 6-week trial studied optimized doses of 0.125 to 0.75 mg/d. At baseline and trial completion, patients were asked question 10 of the International RLS Scale (IRLS): “Overall, how severe is your mood disturbance due to your RLS symptoms – for example, angry, depressed, sad, anxious, or irritable?” Zero signified no disturbance and 4, very severe. All trials were double-blind and placebo-controlled, and patients met all diagnostic criteria of the International RLS Study Group.

Results: Across the three trials, a total of 784 patients contributed analyzable data. At baseline, the mean score was 1.5 in the pramipexole group and 1.7 in the placebo group. At endpoint, the mean response was lowered by 1.0 for pramipexole, compared with 0.7 for placebo. In each trial, the mean reduction was greater for pramipexole, by 0.29 (P=0.1357), 0.32 (P<0.0522), and 0.24 (P=0.0613) in the 3-, 6- and 12-week trials, respectively.

Conclusions: Across three short-term double-blind trials of pramipexole for RLS, the active drug achieved an improvement of mood by one IRLS category, from a baseline mean of mild-to-moderate to an endpoint mean of none-to-mild. The numerical superiority of pramipexole over placebo was consistent across these short-term trials, a benefit that approached significance in the two largest, longest trials.
P2181
DRUG-INDUCED PAROXYSMAL NON-KINESIGENIC DYSKINESIA
Z. Zalyalova, I. Bogdanov
Kazan State Medicine University, Kazan, Russia

We observed paroxysmal non-kinesigenic dystonias in a 17-year-old female patient. Dystonias started 3 weeks after a cancellation of metoclopramid which was admitted for gastritis treatment with duration of 2 weeks at a dose of 10 mg 3 times a day. The attack began from a shiver and started in all the trunk, then trismus and dyskineticus appeared in the lower part of the face with a sluggish shoulders inclination forward and turn of the head to the left. The trunk twisted about its axis and was inclined to the left. Consciousness was thus completely preserved. The patient could be kept in the same position in which she was when the attack started. Speech was disturbed due to compression of the jaw. EEG and MRI did not reveal any pathological changes. During the period of one year attacks did not repeat themselves. However, after a single-pass intramuscular injection of metoclopramid, there was a similar attack. Medicinal paroxysmal non-kinesigenic dystonia was diagnosed. Acute metoclopramid-induced MD were described. The late-onset metoclopramid-induced dystonias were not found in the literature. Medicinal paroxysmal non-kinesigenic dyskinesia is rarely met. Occurrence of metoclopramid-induced dystonias even during treatment is not typical, even more rare are the paroxysmal ones. The paroxysms developed after the long period of time after a cancellation of a drug and could not be described as acute medicinal dystonias. Our case could not be linked to a category of late-onset dystonias. The paroxysms started as a reply to short course of treatment and do not have resistant character.

P2182
BENIGN TREMULOUS PARKINSONISM
E.I. Bogdanov1, Z.A. Zalyalova2
1Department of Neurology, Kazan State Medical University, Kazan, Russia

P2183
SOME PECULIARITIES IN THE DEVELOPMENT OF PARKINSON’S DISEASE
E.I. Kasatkina, N.V. Pizova, M. Tonkaya
Department of Neurology, Yaroslavl State Medical Academy, Yaroslavl, Russia

P2184
CLINICAL AND GENETIC ANALYSIS OF SIX FAMILIES WITH HUNTINGTON’S DISEASE
G.X. Ke1,2, C.F. Liu3, F. Lin4, C.J. Mao5, Y.P. Yang2, Z.H. Qin2
1Department of Neurology, Second Affiliated Hospital of Suzhou University, 2Caducity and Neurology Laboratory of Suzhou University, Suzhou, China

P2185
COGNITIVE IMPAIRMENT AND NEUROSPECIFIC ENOLASE CONCENTRATION IN THE BLOOD SERUM OF PATIENT WITH PARKINSON’S DISEASE
I.A. Zhukova, F.F. Gashilova, V.M. Aliferova, N.G. Zhukova
Department of Neurology and Neurosurgery, Siberian State Medical University, Tomsk, Russia

P2186
RETENTION OF NEW AEDS IN PATIENTS WITH EPILEPSY AND SEVERE LEARNING DISABILITY
J.A. Carpay1, G.A. Graveland2, M. Engelsman1, K. Aalbers1
1Department of Neurology, Tergooiziekenhuis, Blaricum, 2Location Hans Berger, Kempenhaeghe Epilepsy Center, Heeze, SEIN Epilepsy Center, Heemstede, The Netherlands

Purpose: The effectiveness of newly introduced (after 1993) anti-epileptic drugs (AEDs) as add-on medication in patients with severe learning disability and intractable epilepsy is not well documented.

Methods: Retrospective study. We analyzed the medical records of all clients with epilepsy in three institutions for intellectually disabled patients who had ever used at least one of the four new AEDs. We describe the one- and three-year retention rates (Kaplan-Meier method) of lamotrigine (LTG), topiramate (TPM), gabapentin (GBP), and levetiracetam (LEV) in this population. Tiagabin and zonisamide are not licensed in the Netherlands. Pregabalin was licensed in 2005; hence not enough data were available for this drug. Oxcarbazepine was not included in our analysis, because it is often used as a replacement for carbamazepine as first-line AED.

Results: 118 subjects had been using one or more of four new AEDs. Between 2 and 10 (median 6) previous ‘old’ AED regimens/combinations had been tried before prescribing one of the new AEDs. One year retention rates: LTG: 79.2% (N=80); GBP: 66.7% (N=9); TPM: 77.7% (N=32); LEV: 67.7% (N=66). Three years retention rates: LTG: 71.5% (N=67); GBP 42.9% (N=7); TPM: 51.6% (N=28); LEV: 56.1% (N=39). Other clinical data will be included in our presentation.

Discussion: Our retention rate data suggest effectiveness of new AEDs in a substantial proportion of patients with severe learning disabilities and epilepsy, who previously failed to respond to multiple regimens of ‘old’ AEDs.

P2187
SERIAL DAY RAPID KINDLING IS AN EFFECTIVE TOOL IN SCREENING THE ANTI-EPILEPTIC PROPERTIES OF TOPIRAMATE
T. De Smedt, S. De Rouck, R. Raedt, T. Wyckhuys, L. Waterschoot, V. De Herdt, A. Van Dycke, R. El Tahry, K. Vonck, P. Boon
Laboratory for Clinical and Experimental Neurophysiology, University Hospital Ghent, Belgium

Introduction: In this study, a serial day rapid kindling protocol was used to fully kindle rats in a matter of days. Subsequently, the anticonvulsant profile of a relatively new anti-epileptic drug, topiramate, was evaluated in a cross-over design to further validate this rapid kindling model.

Methods: Rats were kindled during three consecutive days, according to the serial day rapid kindling protocol. Topiramate was tested at a dose of 10 mg/kg, i.p., over the next two days using a cross-over design. The stability of the kindled state was evaluated in all rats during two retest paradigms. During the drug-testing procedure, rats received a single i.p. injection of either topiramate or vehicle. Starting one hour later the rats received additional kindling stimulations during which their response was measured.

Results: Serial day rapid kindling induced a long lasting and stable fully kindled state that allowed for the anti-epileptic drug...
screening procedure. Topiramate reduced both the after-discharge-duration and ameliorated seizure semiology in the kindled rats.

**Discussion:** Serial day rapid kindling provided a tool to rapidly kindle rats in three days. Using a cross-over design, clear indications on anti-epileptic activity of a given drug can be determined using few laboratory animals.

**Methods:** Pharmacokinetic data were obtained from 65 patients (aged 4–36 years) taking rufinamide for 84 days during the double-blind phase. Rufinamide was titrated to approximately 45 mg/kg/d over 1–2 weeks. Plasma rufinamide concentrations were determined on days 28 and 84 (or upon withdrawal from the study). Population pharmacokinetic parameters were estimated using a non-linear mixed-effect modelling (NONMEM) by applying a one-compartment model without absorption.

**Results:** The bioavailability of rufinamide decreased with increasing dose (mg/kg). Clearance (CL/F) increased linearly with body surface area (BSA). Age, sex and race had no effect on CL/F. The apparent volume of distribution (Vd/F) was 142 L. The only covariate that appreciably affected exposure to rufinamide was valproate, which reduced rufinamide CL, leading to increases in Cavss. The model predicted that, in typical children (aged 2–12 years) or adolescents (aged 12–17 years) exposed to valproate, rufinamide Cavss would increase approximately by 42% or 17% respectively.

**Conclusions:** As for many other drugs, BSA was the best predictor of rufinamide clearance. Other AED treatments had no significant effects on the PK of rufinamide, with the exception of valproate. Consequently, small reductions in rufinamide dosage might be needed in patients taking valproate.

**Funding:** This work was supported by Eisai.

**Methods:** Concomitant antiepileptic drugs (AEDs) remained stable during an 8-week baseline. Subjects (n=485) reporting at least 8 seizures with no more than 21-days seizure-free were randomized (1:1:1) to placebo, lacosamide 200 or 400 mg/day (bid). Subjects were titrated over 4 weeks by 100 mg/week increments, maintained on treatment for 12 weeks, and transitioned to an open-label trial or discontinued. Efficacy was evaluated with continuous and categorical intent-to-treat analyses of seizure frequency (maintenance vs. baseline). Safety was evaluated with adverse events (AEs), ECGs, vital signs, and clinical laboratory data.

**Results:** Median percent reduction in seizure frequency was 21% (placebo), 35% (200 mg/day), and 36% (400 mg/day). Both 200 and 400 mg/day lacosamide were statistically significant over placebo in reducing seizure frequency from baseline to maintenance (p=0.0223 and 0.0325, respectively). The 50% responder rates were 26% (placebo), 35% (200mg/day), and 41% (400 mg/day). Responder rate over placebo was statistically significant for lacosamide 400 mg/day (p=0.0063). Discontinuation rates for AEs were 6% (placebo), 6% (200 mg/day), and 16% (400 mg/day). The most common (≥10%) in any lacosamide group) AEs were dizziness, headache and diplopia.

**Conclusions:** This trial demonstrated that adjunctive lacosamide (200 and 400 mg/day) was generally well tolerated and produced a statistically significant reduction in seizure frequency in subjects with uncontrolled partial-onset seizures.

**Trial supported by:** SCHWARZ BIOSCIENCES, GmbH.
P2191
AGMATINE ENHANCES THE PROTECTIVE ACTION OF ANTI-EPILEPTIC DRUGS IN THE MOUSE MAXIMAL ELECTROSHTOK SEIZURE MODEL
J.J. Luszczki1, R. Czernecki2, B. Blaszczyk2, S.J. Czuczwar1
1Department of Pathophysiology, Medical University of Lublin, Poland
2Department of Neurology, Neuropsychiatric Hospital, Kielce, Poland

Agmatine is an endogenous amine synthesized by decarboxylation of L-arginine by arginine decarboxylase and hydrolyzed by agmatinase to putrescine. Experimental evidence indicates that agmatine exerts anticonvulsant activity by blocking N-methyl-D-aspartate receptor channels in neurons. At present, agmatine is considered to be a novel neurotransmitter/neuromodulator. The aim of this study was to evaluate the effect of agmatine on the protective action of several conventional and newer antiepileptic drugs (AEDs: carbamazepine, lamotrigine, oxcarbazepine, phenobarbital, phenytoin, topiramate and valproate) in a mouse maximal electroshock seizure (MES) model. Electroconvulsions were produced by an alternating current (25 mA, 50 Hz, 500 V, 0.2 s) delivered via auricular electrodes. Potential adverse effects produced by the combinations of agmatine with AEDs were evaluated in animals challenged with the chimney test (motor coordination), passive avoidance task (long-term memory), and grip-strength test (muscular strength). Results indicate that agmatine significantly enhanced the anticonvulsant effects of phenobarbital and valproate in the MES test, having had no impact on the electroshock action of the remaining AEDs (carbamazepine, lamotrigine, oxcarbazepine, phenytoin and topiramate) in mice. Moreover, all combinations of agmatine with the studied AEDs had no significant effects on motor performance (chimney test), long-term memory (passive avoidance task) and muscular strength (grip-strength test) in mice. Based on this study one can conclude that agmatine potentiated the antiseizure action of phenobarbital and valproate, remaining ineffective when combined with other AEDs. The combinations of agmatine with phenobarbital and valproate may become, in the future, advantageous combinations for patients with epilepsy.

(Supported by a grant DS 475/2006)

P2192
Efficacy of Lamotrigine in Long-term Treatment of Drug-resistant, Partial Epilepsy
Z.J. Martinovic, M.S. Milovanovic, P. Simonovic, N. Buder
Department of Epilepsy, Institute of Mental Health, Belgrade, Serbia

Background and aims: To evaluate the efficacy of add-on lamotrigine (LTM) in drug-resistant, partial epilepsy.

Methods: We carried out a single-centre, open-label, prospective study in adult patients with partial epilepsy resistant to antiepileptic drugs (AEDs) of first and/or second choice. Study protocol consisted of four phases: a 3-month baseline period, a 3-6 month period in which LTG was titrated, a 6-12 month maintenance dosage observation period. Depending on the treatment efficacy and safety, a 9-18 month fourth phase consisted either in change to lamotrigine monotherapy or the change of combination therapy. All patients kept a seizure diary throughout the study and underwent clinical, haematological and electroencephalographic evaluation every 3-6 months.

Results: Patients (61 men and 75 women), aged from 21 to 51, were included in the study. Four of the 174 patients had to stop LTG due to side effects and 25 (19.5%) due to inefficacy. Of 136 patients who completed the study, 32 were rendered seizure free 14 of them with lamotrigine monotherapy. A significant improvement (more than 50% for every type of seizure) occurred in 44.8%. Beneficial effect on mood was found in 22/34 (64.7%) of patients with mood disorders. Clinical factors associated with a better effect were fewer previously used antiepileptic drugs, shorter duration of epilepsy, and combination of lamotrigine with valproate or topiramate.

Conclusions: We have demonstrated a very good long-term retention and efficacy of lamotrigine adjunctive therapy in drug-resistant, partial epilepsy and defined some factors associated with a favourable outcome.

P2193
Randomized Dose-controlled Multicenter Study of Topiramate as First-line Therapy in Adolescents with Epilepsy – a Post-hoc Analysis (EPMN-106/INT-28)
B. Schaulbe1, S. Wang2, F. Wiegand1
1Department of Medical and Scientific Affairs, Janssen-Cilag GmbH, Neuss, Germany, 2Department of Statistics, Johnson & Johnson Research and Development L.L.C., 3Department of Clinical Development, Ortho McNeil Neurologics, Titusville, NJ, USA

Objectives: Analyses of data on adolescent subjects from dose-controlled studies evaluating the efficacy and tolerability of topiramate as initial monotherapy.

Methods: Subset analyses of a previously published trial including patients aged 10–15 years with newly diagnosed epilepsy and untreated patients with epilepsy relapse and >2 lifetime seizures and 1–2 partial or GTC seizure during a 3-months retrospective baseline. Primary efficacy endpoint was time to first seizure; secondary efficacy measure was seizure free rate at 6 months and 1 year. The safety population was pooled with patients receiving 50 mg/day in a very similar pivotal trial.

Results: A total of 470 patients were included in the initial efficacy analysis, 114 patients between 10–15 years of age (50% female) are presented here. Kaplan-Meier survival analysis for time to first seizure in the adolescent subset of the IIT population favoured 400 mg/day (n=57) over 50 mg/day (n=57) (p=0.001). The probability of being seizure-free at 6 months was 79% in those randomized to 50mg/day and 94% in patients randomized to 400 mg/day (p=0.001). Average topiramate dose/day during the double blind phase was 43 mg/day (0.92 mg/kg/day) in the 50 mg group and 335 mg/day (7.47 mg/kg/day) in the 400 mg/day group. Adverse events leading to study discontinuation were anxiety, chest pain and migraine in one patient in the 50 mg arm. In the 400 mg arm, 7 patients overall discontinued due to cognitive problems, fatigue and mood complaints.

Conclusion: Results of these analyses support the efficacy and safety of topiramate for initial monotherapy of partial-onset or generalized tonic-clonic seizures in adolescents with epilepsy.

P2194
Effectiveness of Topiramate Across Age Groups in Elderly Patients with Epilepsy – Results of an Open-label, Phase IV Clinical Trial
H. Stefan1, A. Schreiner2, B. Schaulbe1
1Epilepsy Center, University of Erlangen, 2Department of Medical and Scientific Affairs EMEA, 3Department of Medical and Scientific Affairs, Janssen-Cilag GmbH, Neuss, Germany

Objective: To assess effectiveness of topiramate (Topamax®, TPM) in different age groups in elderly (≥60) with epilepsy.
Methods: Open label, multicentre phase IV flexible dose clinical trial including elderly (60–64, 65–74 and ≥75 years) with epilepsy were followed for a median of 12 months. Seizure frequency and adverse events were assessed at each visit.

Results: 107 patients (53% male, mean age 69±7 years) were enrolled. 102 patients had at least one seizure during the retrospective 12-week baseline (GTC in 58%, complex partial in 25%). Seizure frequency was highest in the oldest group (9.3±34.1 at baseline). Mean duration of epilepsy was 11.8, 9.7 and 5.5 years, respectively. Mean seizure frequency for all was 3.5±14.6 at baseline and decreased to 1.6±7.7 at endpoint (p<0.0001). Mean monotherapy dose was lowest in the oldest group (86 mg/day). The proportion of responders (seizure reduction ≥50%) was highest in the youngest group (87% responders). Overall, 78% of patients were responders and 44% remained seizure-free throughout the study.

46 patients (43%) had at least one treatment-emergent adverse event (TEAE). The number of TEAEs was highest amongst the oldest elderly. TEAEs ≥5%: somnolence (9.4%), dizziness (7.5%), paraesthesia (5.6%), memory difficulties 5.6%. Main reasons for study discontinuation: TEAE (15.9%), loss to follow-up (12.2%).

Conclusion: In elderly patients with epilepsy, TPM was well tolerated amongst all age groups, and was associated with a significant decrease in seizure frequency. Doses used were slightly lower than the recommended target doses for adults.

P2195
SYNERGISM OF LACOSAMIDE WITH ESTABLISHED ANTI-EPILEPTIC DRUGS IN THE 6Hz SEIZURE MODEL IN MICE
A. Shandra1, P. Shandra2, O. Kaschenko1, T. Stoehr1
1Odessa State Medical University, 2Odessa National University, Odessa, Ukraine, 1Department of Pharmacology and Toxicology, Schwarz Biosciences, Monheim, Germany

Purpose: Lacosamide (LCM) is a functionalized amino acid with a novel dual mode of action: enhancement of sodium channel slow inactivation and modulation of collapsin response mediator protein 2. Due to this novel mode of action lacosamide has the potential to act additively or even synergistically with other antiepileptic drugs (AEDs). New AEDs are initially licensed as add-on treatment, often with no evidence to suggest which existing drugs they should be employed with. The objective of this study was the evaluation of the interaction between LCM and a number of other AEDs by isobolographic analysis.

Methods: The anticonvulsant effect of LCM with other AEDs (carbamazepine (CBZ), phenytoin (PHT), valproate (VPA), lamotrigine (LTG), topiramate (TPM), gabapentin (GBP) and levetiracetam (LEV)) at fixed ratios of 1:3, 1:1 and 3:1 was evaluated in the 6Hz-induced seizure model in mice. The protective action of an AED was defined as the absence of seizures.

Results: All studied AEDs produced dose-dependent anticonvulsant effects against 6 Hz induced seizures. Combinations of LCM with CBZ, LTG, TPM, GBP or LEV were supra-additive (synergistic). All other LCM/AED combinations displayed additive effects with a tendency towards supra-additivity. Furthermore, no enhanced adverse effects were induced by combinations of LCM with these AEDs as assessed in the rotorod test.

Conclusions: The isobolographic analysis revealed that combinations of LCM with first-generation (CBZ) or novel AEDs (TPM, GBP, LTG or LEV) are associated with synergistic anticonvulsant effects. Similar but less profound synergistic effects were seen with LCM in combination with PHT or VPA.

P2196
IN_involved_in_the_anticonvulsant_effect_of_angiotensin_iV_against_pilocarpine-induced_limibic_seizures_in_rats
B. Stragier, R. Clinkers, A. Meurs, D. De Bundel, S. Sarre, G. Ebinger, Y. Michotte, L. Snoedlers
Department of Pharmaceutical Chemistry, Drug Analysis and Drug Information, Research Group Experimental Pharmacology, Vrije Universiteit Brussel, Belgium

The renin-angiotensin system is a powerful hormonal system, involving a number of bioactive peptides. Among these, angiotensin IV (Ang IV) gained a lot of interest since it is able to interfere with different brain functions such as learning and memory. In this study, we evaluated the anticonvulsant properties of Ang IV in the acute pilocarpine rat seizure model. Simultaneously, the neurochemical changes in the hippocampus were monitored using in vivo microdialysis coupled to microbore liquid chromatography. Intracerebroventricularly (i.c.v.) administered Ang IV protected rats against seizures and caused a significant increase in the hippocampal extracellular dopamine and serotonin levels. Ang IV is an inhibitor of insulin-regulated aminopeptidase (IRAP), which metabolises different neuropeptides such as somatostatin-14, vasopressin and oxytocin. Among these, somatostatin-14 is presumed to have anticonvulsant effects. Indeed, i.c.v. administered somatostatin-14 also protected rats against seizures and caused increases of the hippocampal dopamine and serotonin levels. Moreover, the anticonvulsant effect as well as the increases of dopamine and serotonin induced by Ang IV could be blocked by concomitant i.c.v. administration of the somatostatin receptor 2 antagonist cymamide 154806. These results reveal a possible role for dopamine and serotonin in the anticonvulsant effect of Ang IV and somatostatin-14. Our study shows that the ability of Ang IV to inhibit pilocarpine-induced convulsions is dependent on somatostatin receptor 2 activation and is possibly mediated via inhibition of IRAP resulting in an elevated concentration of somatostatin-14 in the brain.

P2197
LOW POTENTIAL FOR DRUG-DRUG-INTERACTION OF LACOSAMIDE
D. Thomas1, U. Scharfeneccker1, B. Nickel1, P. Doty2, W. Cawello1, R. Horstmann1
1Department of Clinical Development, Schwarz BioSciences GmbH, Monheim, Germany, 2Department of Clinical Development, Schwarz BioSciences Inc., Raleigh, NC, USA

Lacosamide is a new drug being developed for the treatment of epilepsy and neuropathic pain. Information about the pharmacokinetic drug-drug-interaction (DDI) potential of lacosamide is an important part of its safety profile. Regarding the DDI potential the results of several preclinical studies as well as of 9 phase 1 trials (n=184 subjects) and a phase 2 trial (n=91 patients) are presented. In vitro, lacosamide is not substantially metabolized and shows no or low potential to inhibit or to induce CYP isozymes. Since lacosamide has low binding to plasma proteins (<15%), drug displacement interactions are unlikely. Lacosamide was administered to extensive and poor metabolizers of CYP2C19 and the results showed that CYP2C19 has no clinically relevant effect on the metabolic fate of lacosamide. Further DDI trials have been performed with the antiepileptic drugs carbamazepine (inducer of CYP450 system) and valproic acid (inhibitor of CYP450 system) under steady-state conditions. In these trials, lacosamide had no
influence on rate or extent of absorption of carbamazepine or valproic acid and vice versa. DDI trials with digoxin, omeprazole and metformin showed no relevant influence of these drugs on lacosamide and vice versa. Lacosamide did not influence the pharmacokinetics and pharmacodynamics of the oral contraceptive Microgynon® (containing 0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel). Coadministration of food did not alter the rate or extent of gastrointestinal absorption of lacosamide. No DDI have been observed in these studies. Therefore the data suggest that lacosamide has low potential for DDI in clinical use.

Results: Administration of Carbamazepine results in increasing of second stage duration by 49.6%, decreasing of the fast stages duration by 18.1%. Deep stages were increased by 28.8%. Valproic acid disrupted sleep by increasing stage 1 sleep (16.8±9.8%; control: 7.7±4.8%) without influence on other stages. Gabapentin improved sleep by increasing slow wave sleep (SWS) – 19.4±4.2%; control: 11.3±4.4%);

Conclusions: AEDs have differing effects on sleep structure, which can be beneficial or detrimental. Consideration of these potential effects is important in maintaining optimal sleep in patients with epilepsy.

P2200

PREGABALIN 300 MG/D IS EFFICACIOUS AND WELL TOLERATED AS ADJUNCTIVE THERAPY FOR PARTIAL SEIZURES: ANALYSIS OF DATA FROM 2 RANDOMIZED CLINICAL TRIALS

F. Baldinetti, T. Leon, B. Emir, E. Whalen
Pfizer Global Pharmaceuticals, New York, NY, USA

Objective: Pregabalin (150–600 mg/d) is approved in the US, EU, and elsewhere as adjunct therapy for adult patients with partial-onset seizures. We evaluated the efficacy, safety, and tolerability of pregabalin at 300 mg/d by combining data from 2 randomized clinical trials (RCTs) that included 300 mg/d pregabalin fixed-dosage arms.

Methods: The 2 RCTs shared a similar parallel-group design, treatment was administered over 11 weeks. 242 patients received pregabalin 300 mg/d, 240 received placebo. Patients were ≥12 years of age, and refractory to treatment. The primary efficacy measure was reduction in seizure frequency compared with baseline. A secondary efficacy measure was responder rate (patients who experienced seizure reductions ≥50% during treatment versus baseline).

Results: The pregabalin 300 mg/d group demonstrated a significant reduction in seizure frequency relative to placebo; the treatment difference between pregabalin and placebo in mean seizure reduction was 34.8 (p<0.0001). Overall, 36% of patients receiving 300 mg/d pregabalin responded compared with 20% of patients receiving placebo (P<0.05). Adverse events (AEs) associated with 300 mg/d pregabalin were typically mild to moderate, tended to resolve with time, and included: dizziness (14% vs. 4.6%), somnolence (7.4% vs. 5%), and weight gain (3.7% vs. 0%)/ (300 mg/d pregabalin vs. placebo).

Conclusions: Pregabalin 300 mg/d was efficacious and generally well-tolerated. At 300 mg/d, 36% of patients responded to pregabalin treatment. However, as previously reported, some patients may require, and tolerate well, increased dosages up to 600 mg/d. Study funded by Pfizer.

P2201

EFFECTS OF THREE CALCIUM CHANNEL ANTAGONISTS (AMLODIPINE, DILTIAZEM AND VERAPAMIL) ON THE PROTECTIVE ACTION OF TOPIRAMATE AGAINST MAXIMAL ELECTRO-SHOCK-INDUCED SEIZURES IN MICE

S.J. Czuczwar1, 2, M. Trojanar1, M. Trojanar, B. Szostakiewicz3, J.J. Luszczki1

1Department of Pathophysiology, Medical University of Lublin,
2Department of Physiopathology, Institute of Agricultural Medicine, Lublin, Poland

The pathophysiology of epileptic seizures is complex and calcium ions are likely to play an important role in this regard. Experiment-
al evidence indicates that calcium channel antagonists possess anti-convulsive potential in many seizure models, including the maximal electroshock seizure (MES) test in mice. The aim of this study was to assess the effects of three calcium channel blockers (amlodipine, diltiazem, and verapamil) on the antielectroshock action of topiramate (TPM) in mice. The anticonvulsant effects of TPM and its combination with three calcium channel blockers were determined in the MES model in mice. Electroconvulsions were produced by an alternating current (25 mA, 50 Hz, 500 V, 0.2 s) delivered via auricular electrodes. Potential acute adverse effects of TPM administered alone and in combination with calcium channel blockers were studied in the chimney test in mice. Results indicate that amlodipine (20 mg/kg) potentiated the anti-seizure effect of TPM against MES-induced seizures. Similarly, diltiazem (5 mg/kg) significantly enhanced the antielectroshock activity of TPM in mice. In contrast, verapamil (20 mg/kg) did not affect the anticonvulsant properties of TPM in the MES test. The evaluation of acute adverse effects of TPM in the chimney test revealed that amlodipine, diltiazem and verapamil had no impact on TPM-induced motor coordination in mice. In conclusion, one can ascertain that the combinations of TPM with amlodipine and diltiazem may occur advantageous for epileptic patients treated with these drugs for other than epilepsy reasons. Only the combination of verapamil with TPM was neutral from a preclinical point of view.

(Supported by KBN 2P05D09629).

**P2202**

**THE EVALUATION OF THE PHARMACOLOGICAL MANAGEMENT OF EPILEPSY WITHIN AN OUTPATIENT SETTING OF MONTENEGRO: A PHARMACO-EPIDEMILOGICAL ASPECT**

N. Duborija-Kovacevic1, S.M. Vujisic2, Z. Glomazic, Z. Tomic1

1Department of Pharmacology, University of Montenegro Medical School, 2Institute of Neurology, Clinical Centre of Montenegro, The Republic Health Insurance Fund of Montenegro, Podgorica, Montenegro, 1Department of Pharmacology, Toxicology and Clinical Pharmacology, Novi Sad University Medical School, Novi Sad, Serbia

**Objective:** The aim of our study was to evaluate the pharmacological management of epilepsy within outpatient setting of Montenegro during a one-year period and to estimate its compatibility with actual guidelines.

**Methods:** For the evaluation of pharmacological management of epilepsy we used a computerized report from the Health Insurance Fund of Montenegro, which comprised all antiepileptic drugs (AEDs) (ATC code N03) that were prescribed during 2005 for the treatment of epilepsy (ICD code G40) within outpatient setting. Our results were expressed as the number of defined daily doses per 1000 inhabitants per day (DTDs) and percentages. The population of Montenegro was approximately 660,000 during the investigated period. All AEDs were classified according to internationally accepted anatomic-therapeutic-chemical (ATC) classification of drugs.

**Results:** The overall prescribing of AEDs (N03) within outpatient setting of Montenegro during the investigated period was 2.85 DTDs (100%). Older barbiturate derive phenobarbital (N03AA02) was the most common prescribed drug (1.76 DTDs, 62%), followed by standard antiepileptic carbamazepine (N03AF01) (0.55 DTDs, 19%). The combination of sodium-valproate and valproic acid (N03AG02) was in the third place (0.36 DTDs, 13%). Newer antiepileptic agent, lamotrigin (N03AX09), was prescribed in less than 4% (0.11 DTDs). The number of other drugs in total AEDs prescribed was almost 2% (0.07 DTDs).

**Conclusions:** Montenegrin physicians mostly prescribed the second-line AED phenobarbital, with complex pharmacokinetics and side-effects, but with wide availability, long-term experience, and also, lower price in comparison to newer drugs. This was probably the consequence of many medical and non-medical influences.

**P2203**

**PERI-ICTAL WATER DRINKING: A GOOD LOCALISING AND LATERALISING OF NON DOMINANT TEMPORAL LOBE EPILEPSY, TWO CASE REPORTS AND REVIEW OF THE LITERATURE**

L. Errguig, F. Lahjuoui, H. BELAIDI, N. Brouk, B. Kably, R. Ouazzani

Department of Clinical Neurophysiology, Hôpital des Spécialités, Rabat, Morocco

Peri-ictal behaviour disorders can be helpful in localising and lateralising seizure onset in partial epilepsies, especially those originating in the temporal lobe. In this paper, the authors present the case of two right-handed women aged 30 and 40 years who presented with partial seizures of mesial temporal type. Both of the patients had drug resistant epilepsy and undergone presurgical evaluation tests including brain magnetic resonance imaging, video-EEG monitoring and neuropsychological testing. The two patients had hippocampal sclerosis in the right temporal lobe and exhibited peri-ictal water drinking (PIWD) behaviour concomitant with right temporal lobe discharges documented during video-EEG recordings. Anterior temporal lobectomy was performed in one case with an excellent outcome after surgery. She is free of seizures at 12 months of follow-up. The authors review other peri-ictal autonomic symptoms published as having a lateralising significance such as peri-ictal vomiting, urinary urge, ictal piloerection, etc. It is very important to search for these symptoms, even if not spontaneously reported by the patient, because they are often under-estimated by the patients themselves and also by physicians. Additionally, patients with lateralising auras during seizures have a significantly better outcome after epilepsy surgery than those without lateralising features.

**P2204**

**EPILEPTIC AND NON-EPILEPTIC SEIZURES WITH DROPPED HEAD SYNDROME IN ONE PATIENT: SINGLE ENTITY OR ORGANIC AND PSYCHOGENIC CO-MORBIDITY?**

K. Farmíková, P. Kaňovský, J. Burešová, M. Labounek, E. Obržázková, R. Mačák, Č. Šišar

Department of Neurology, Palacky University and University Hospital, Olomouc, Czech Republic

**Purpose:** To evaluate the possibility that previously described dropped head syndrome (Brázdil et al. 2005) is a unique symptom of a syndrome with both epileptic and non-epileptic seizures, and not only presumed focal myopathy.

**Method:** Video-EEG study with non-invasive and semi-invasive recordings together with EMG examination was used to evaluate the character of dropped head syndrome in a patient with mental retardation, who suffered from a syndrome manifesting both epileptic and non-epileptic seizures. The patient was a 29-year-old female with mental retardation, suffering from GTCS (sporadic night seizures without focal onset) starting in childhood and with interictal focus of epileptic activity in the right F-C region; treated with CBZ and later with VPA. Within the last year a new type of seizures occurred, with nausea, paroxysmal vertigo, loss of contact
and lack of consciousness resembling absence seizures, lasting 5–10 minutes, without any correlate in the EEG. Together with the seizures a dropped head sign appeared, with complete normalization of head posture when the seizure disappeared.

**Results:** The complete non-invasive and semi-invasive video EEG-monitoring has shown evidence that the first type of seizure had an epileptic origin, and the second one non-epileptic. The EMG found no abnormality when the needle examination of surface and deep neck muscles examination was done.

**Conclusion:** The dropped head syndrome, present in a patient with mental retardation and suffering from both epileptic and non-epileptic seizures, need not be a symptom of focal myopathy due to VPA use. It is rather a feature of the non-epileptic seizure.

**P2205**

**CORRELATION OF SERUM LEVEL OF ANTIEPILEPTIC DRUGS (AEDS) AND COMPLIANCE IN PATIENTS WITH EPILEPSY IN THE EAST-HUNGARIAN EPILEPSY DATABASE**

I. Fekete1, 2, S. Puskas1, E. Cso2, K. Fekete1, E. Barna1, B. Vamosi1, L. Horvath1

1Department of Neurology, University of Debrecen, 2Central Pharmacy, University of Debrecen, Hungary

**Background:** The doses of AEDs must be adjusted individually due to the great variability in different epileptic syndromes and intra- and interindividual responses. The monitoring of AEDs’ serum level might be useful for clinicians.

**Methods:** At the Debrecen Epilepsy Database we tested the correlation between AEDs’ serum value and patients’ compliance.

**Results:** 342 patients underwent serum antiepileptic level examination. 397 patients had monotherapy, 27 had bitherapy- or polytherapy. Carbamazepine (CBZ) serum level was examined in 281 patients and it was within normal range (6–12 mg/L) in 164 patients (58%). The compliance was good in 82% of the patients. The serum level was below normal in 112 patients (40%), but the compliance was good in 83%. Valproate (VPA) serum level was examined in 108 patients, and it was within normal range (30–120 mg/L) in 96 patients (89%), with good compliance (73%). The low and high serum VPA concentration was not caused by bad compliance (70% and 100%). In case of CBZ and VPA combination (27 patients), it was characteristic that one of the AEDs was below normal serum value with good compliance (90%), but it was bad if both of them were low-level (19%). We had 8 patients on phenytoin therapy – 5 patients’ serum level was below 10 mg/L, and they had bad compliance.

**Conclusion:** The relatively low serum AED concentration was not caused by bad compliance. In selected cases, particularly during combination therapy with enzyme-inducing agents serum level can be valuable but single measurement must be interpreted cautiously.

**P2206**

**EPILEPTOGENIC KLUVER-BUCY SYNDROME (EKBS) TREATED WITH NASOGASTRIC LEVETIRACETAM (LVT) AS ADJUNCTIVE THERAPY: A CASE OF EXCELLENT NEUROLOGICAL RECOVERY AT 4 MONTHS AFTER DISCHARGE**


Department of Neuroscience, Azienda Ospedaliera, Benevento, Italy

**Purpose:** To assess the efficacy of LVT as an adjunctive therapy in a case of EKBS.

**Methods:** An epileptic 11-year-old girl, who suffered from herpetic encephalitis at age of three, treated by lamotrigine 300 mg, clonazepam 1.5 mg, phenobarbital (PHB) 50 mg, and sodium valproate (VLP) 1000 mg daily, was admitted because of myoclonic and generalized tonic-clonic seizures. She had visual agnosia, aphasia, meekness, sexual masturbation, and hyperorality. Nasogastric treatment was started with VLP 1600 to 2400 mg/day, oxcarbazepine (OXC) 1500 mg titrated 300 mg/day, while PHB was interrupted. Because of severe hepatic side effects, VLP was suspended. Because of convergent strabismus OXC was reduced to 900 mg/day and LVT 2000 mg/day was started with a further increase to 3000 mg the day after.

**Results:** After LVT was added we observed complete remission of the seizures, masturbations and hyperorality. She improved the meekness and showed a better attention and a better level of consciousness which enabled a psychological approach. Rachicentesis was negative for searching viral DNA/RNA. MRI DW/PW showed signs of previous right cerebellitis. SPECT showed hypoperfusion in the left temporal lobe. EEGs showed an epileptogenic focus in the right centro-temporal area. No crisis and aphasia was referred 4 months later although she was not able to perform the Raven’s matrix test.

**Conclusions:** We suggest that this case of EKBS may have originated from a diachisis phenomenon provoked by the right cerebellitis. LVT as an adjunctive therapy was associated with remission of seizures and improvement in neurological status.

**P2207**

**SEIZURE FREEDOM AS A FUNCTION OF BASELINE SEIZURE FREQUENCY (BSF) IN PREGABALIN TRIALS**

J. French1, R. Benabou2, E. Whalen2, T. Leon1, F. Baldinetti2

1University of Pennsylvania Medical Epilepsy Center, Philadelphia, PA, 2Pfizer Global Pharmaceuticals, New York, NY, USA

**Objective:** To evaluate seizure freedom as a function of BSF in patients receiving pregabalin or placebo.

**Background:** Pregabalin has demonstrated efficacy as add-on treatment of partial seizures in 5 randomized controlled trials (RCTs).

**Design and methods:** Data were pooled from 5 similarly designed RCTs of pregabalin as add-on treatment for partial seizures. Seizure activity was measured in BSF using patients who were randomized and treated with either pregabalin 600 mg/d or placebo for 12–20 weeks. Patients’ BSF was transformed to the log-scale. Seizure freedom was analyzed within treatment with the BSF as a predictor. Linear logistic regression and non-parametric smoothing methods were applied to explore the degree of relationship with baseline in patients who completed study treatment. This relationship was also explored in non-completers.

**Results:** 1039 patients were included in the analysis: 532 on pregabalin 600 mg/d; 507 on placebo. Median BSF was 10.0/month (range, 2-436) for pregabalin and 9.0/month (range, 0-3357) for placebo. 74% of patients were on ≥2 AEDs. Among the 366 patients who completed pregabalin treatment, 11 were seizure free. Two of 413 placebo completers were seizure free. Analyses suggest that greater baseline seizure frequency is associated with decreased seizure freedom in the pregabalin group (nominal p<0.05). Non-parametric estimates of seizure freedom for pregabalin were 5.5%, 1.3%, and 0.4% for baseline seizure frequencies of 5, 10, and 15 respectively.

**Conclusions and relevance:** Increased baseline seizure frequency is associated with reduced likelihood of seizure freedom. Administration of pregabalin 600 mg/d increased the likelihood of patients becoming seizure free.

Study funded by Pfizer, Inc
P2208
CRYPTOGENIC VERSUS SYMPTOMATIC WEST SYNDROME
M. Gandea, O. Tarta-Arsene, S. Magureanu
Department of Paediatric Neurology, Clinical Hospital, Bucharest, Romania

Aim: To compare evolution and prognosis of cryptogenic versus symptomatic West syndrome.

Methods: It has been evaluated using all patients’ charts diagnosed with West syndrome in our department during 2001–2003. All patients with cerebral affection were diagnosed as having symptomatic syndrome, compared with those with normal neuroimaging – cryptogenic. They were evaluated according to clinical (neurological, seizures, psychological) and investigation (EEG, CT, IRM) evolution between 4–6 years.

Results: West syndrome was diagnosed in 17 patients (ages between 3 and 10 months), 8 patients with symptomatic syndrome and 9 patients with cryptogenic syndrome. At the debut of study, 4 patients with symptomatic syndrome had asymmetrical spasms, with focal epileptiform discharges, compared with all with cryptogenic syndromes that had symmetrical spasms and hypsarrhythmia. All patients were treated with antiepileptic (valproate, topiramate, and benzodiazepine) and corticosteroids, but with different therapeutic schemes. The seizures were controlled in 5 patients with symptomatic syndrome (those with symmetrical spasms and one patient with tuberous sclerosis) and in 7 patients with cryptogenic syndrome. All patients had mild to severe mental retardation.

Conclusions:
1. Symptomatic West syndrome with asymmetrical spasms and focal EEG could be a better prognostic factor for West syndrome; 2. Even though the seizures were controlled, the mental evolution was poor.
3. Symptomatic West syndrome had worse prognostic and did not respond in a positive way to treatment compared with cryptogenic syndrome.
4. To confirm these hypothesis larger comparative studies are necessary.

P2209
THE DIAGNOSTIC VALUE OF PROLONGED VIDEO EEG (TELEMETRY) IN IDENTIFYING PAROXYSMAL NON-EPILEPTIC EVENTS IN CHILDREN WITH EPILEPSY
J.A. Gosalakalak, N. Hussain
Department of Paediatric Neurology, University Hospitals of Leicester, UK

Introduction: Epilepsy and behaviour that can be confused with epileptic seizures are common in children.

Aim: To report on the usefulness of adding video telemetry to routine EEG studies of epileptic children with frequent atypical paroxysmal events.

Results: Age of the patient ranged from 1 to 15 years (mean: 7 years, median age: 8.5 yrs). The mean length of stay was 2.5 days (range: 1–5 days). Paroxysmal events were analysed. 884 (54%) were non-epileptic. We identified epileptic seizures in 33 (75%) children, non-epileptic events in only 11 children (25%), and both epileptic and non-epileptic events in 25 children (57%). A diagnosis of a specific non-epileptic event was confirmed in 55% of cases. Epilepsy classification was changed in 8 children after video-EEG.

Discussion: Our study identified 54% of the paroxysmal events as being non-epileptic, and staring was the most common non-epileptic event (32%), which was higher than in previous studies (12–40%) (3, 4). Recognition of non-epileptic events had a significant impact on treatment plans and helped us to counsel parents about the true nature of the paroxysmal events.

Conclusion: Paroxysmal non-epileptic events can cause diagnostic confusion, particularly in children with developmental delay, epilepsy (especially refractory epilepsy). Accurate diagnosis can be obtained in the majority of cases using prolonged video EEG monitoring.

P2210
THE EFFECTS OF EPILEPSY ON LATE COMPONENTS OF EVENT RELATED POTENTIAL AND REACTION TIME
V.P. Ivetic, O.F. Barak, O.S. Ivetic
Department of Physiology, Medical Faculty, Novi Sad, Serbia

Purpose: The effects of epilepsy on late component (P300) event related potential (ERP) and reaction time (RT), were investigated.

Material and methods: 40 subjects aged between 18 and 22 (mean 22.4) participated in the investigation. 20 female patients with idiopathic generalized epilepsy were compared with controls – 20 healthy female persons. P300 event related potential was determined using oddball paradigm. The group analysis of P300 latency and amplitude was undertaken across the two midline sites (Fz and Cz, 10/20 system).

Results: P300 latency was increased in patients with chronic epilepsy but not significantly. There was no relation between P300 latency and amplitude with seizure onset, duration frequency. Also no significant associations were found between P300 amplitudes in a group of female subjects with epilepsy. However, epileptic persons showed decreased P300 amplitude but not significantly as compared with healthy persons. Significantly faster RT were found in healthy persons compared with our patients (p=0.2). The mean RT and standard deviation (SD) in healthy persons was 295 ms and ±0.4 (SD), in epileptic patients. The mean RT was 321 ms and SD±1.3. Patients with abnormal EEG had significantly prolonged RT to those with normal EEG. In epileptic persons, results obtained showed significant positive correlations between duration of RT and P300 latency. These findings suggest that epilepsy had effects on late components of event related potential and reaction time.

P2211
MIDDLE CEREBRAL ARTERY ISCHEMIA AND SEIZURE SUSCEPTIBILITY
D.S. Jung, K.D. Choi, K.P. Park, J.H. Choi, Y.J. Yoon
Department of Neurology, Pusan National University School of Medicine, Pusan, South Korea

Background and aims: Post-ischemic stroke (PS) seizures have been defined as those either at the beginning of or after cerebral infarction in patients without a history of seizure disorder. The main objectives were to determine the relationship between ischemic injury and seizure susceptibility.

Methods: In the first phase, after ischemia by intraluminal monofilament technique, animals were killed with repeated daily administration of pentyleneetrazole (PTZ, 10, 30 mg/kg, i.p.) for 5 days. In the second phase, in the indomethacin group, after ischemia by photothermbotic method, injection of indomethacin (2.5 mg/kg, i.p.), twice a day for 6 days, from the 7th day, and then kindled with repeated daily administration of PTZ (30 mg/kg, i.p.) for 4 weeks. In the retinoic acid group, injections of retinoic acid (5 mg/kg, i.p.) once a day for 6 days after ischemia, and then from the 7th day, kindled with repeated daily administration of PTZ (30 mg/kg, i.p.) for 4 weeks.
**Results:** The present study showed PTZ-induced kindling was markedly augmented in the group of transient MCA occlusion. The increment of kindling scores in transient focal cerebral ischemia may reveal that the brain in a PS seizures model increases excitability. In the Indomethacin and Retinoic acid group, the PTZ-induced kindling scores were altered after the 7th day in comparison with control and ischemia group, showing lower seizure susceptibility than in the ischemia only group.

**Conclusion:** This result prompted us to assume that the late post ischemic injury process may contribute to increased inhibition rather than excitation in regard to inflammation.

---

**P2212**

**ARE SUBJECTS WITH EPILEPTIC SEIZURES AND SUBJECTS WITH SYCONE FITS ALWAYS DIFFERENT PATIENTS?**

V.A. Karlov, T.S. Sologubova

*Department of Neurology, Moscow State Medical Stomatological University, Moscow, Russia*

**Purpose:** Epileptic seizures and syncope are the most prevalent paroxysmal events in neurological clinical practices. Patients with unresolved diagnosis were investigated.

**Method:** 52 patients (29 females, 23 males) with repeated fits were studies. The mean age was 30.7±16.6 years. There was a control group of 16 healthy men. The following methods were used: prolonged passive orthostatic trial on the special table with ECG, EEG registration (Tilt test); EEG after 24 hour sleep deprivation, polygraphic registration of night sleep. EEG analysis also included calculation of the overall power and separately, all basic rhythms.

**Results:** Patients were selected by: 1) syncope (23 p), 2) epileptic seizures (11 p), 3) combination of both of them (13 p) – all 47 patients (90.3%). In 5 patients (9.3%) an accurate diagnosis was not determined. Tilt test was more effective as a diagnostic tool for determining syncope: it diagnosed 63.9% syncope cases vs. only 7.7% epileptic seizures, while long polygraphic sleep and video EEG monitoring was more effective for epileptic seizures: 52% showed positive results. The combination group had some clinical peculiarities. EEG analysis revealed in all patient groups substantial increase of EEG power, separately teta-delta band.

**Conclusion:** Patients with unresolved differential diagnosis between syncope and epileptic seizures resulted in accurate diagnosis in 90.3% patients. It also differentiated between the patient group with combination of syncope and epileptic seizures, which has shown clinical peculiarity. There is a common mechanism that promotes cerebral paroxysmal events – increase of EEG power and shift bands to the left.

---

**P2213**

**THE INFLUENCE OF ANTI-EPILEPTIC DRUGS (AEDS) ON THE REVEALING OF OSTEOPOROSIS**

A. Karp-Majewska, B. Adamkiewicz, A. Klimek

*Department of Neurology and Epileptology, II Department of Nervous System Diseases, Lodz, Poland*

Osteoporosis is a generalized disease of the skeleton, characterized by low bone mineral density and disturbance of microarchitecture. One of the most significant features leading to osteoporosis is treatment with AED. Nowadays the most popular diagnostic method is dual energy X-ray absorptiometry (DEXA). Yet it reveals advanced level of osteoporosis, which cannot be reversed. Thus there is a need for diagnosis development of new markers of bone metabolism. The aim of this paper is to find out whether osteoporosis can already appear after a few years of treatment with AED and which marker is the most effective. The studies were conducted in a group of 45 patients aged 20–50 treated over 2 years with AED and in the control group – 30 persons properly chosen in respect to age and sex. The patients were examined by DXA and bone markers: CTX (Collagen Type And Crosslinked C-telopeptide) and osteocalcin. Based on DXA and bone markers in 23 (51.1%) persons taking AED we found osteopenia or osteoporosis. DXA showed it in 19 persons (42.2%), increase level of CTX in 21 persons (46.6%), and osteocalcin in 14 person (31.0%). In the control group we found only 5 persons with osteopenia, and no osteoporosis. DXA and CTX revealed osteopenia in all 5 persons, but increased level of osteocalcin was found in 3 persons only (10.0%). Long-term using of AED has a large influence in decrease of BMD. BMD is dependent proportionally on the length of taking an AED and their kind. CTX is the most sensitive, the weaker is DXA and osteocalcin the least.

---

**P2215**

**CHANGES IN INTERICTAL CEREBRAL BLOOD FLOW IN PATIENTS WITH EPILEPSY**

K.S. Kim, M.J. Kim, J.K. Kim, B.G. Yoo

*Department of Neurology, Kosin University College of Medicine, Busan, South Korea*

**Purpose:** To evaluate the cerebral hemodynamic changes during the interictal period in patients with epilepsy, we investigated changes in cerebral blood flow velocities by transcranial Doppler sonography (TCD).
Methods: Blood flow velocities and pulsatility indices were measured in both anterior cerebral arteries, middle cerebral arteries, posterior cerebral arteries, internal carotid arteries, and basilar artery using TCD in 21 patients with epilepsy and 21 age and sex matched normal adults. We also evaluated the effects of seizure type, seizure frequency, EEG findings, and anticonvulsant medication on cerebral blood flow velocities.

Results: The blood flow velocities of cerebral arteries were decreased in the patients, but the pulsatility indices were not different. Cerebral blood flow velocities were influenced by seizure type, EEG findings, or anticonvulsant medication.

Conclusion: This study demonstrates that cerebral blood flow velocities might be decreased during interictal period in patients with epilepsy, and suggests that TCD is a useful method for the investigation of the cerebral hemodynamic changes in epilepsy.

P2216
EFFICACY AND TOLERABILITY OF LEVETIRACETAM DURING ONE-YEAR FOLLOW-UP AS ADD-ON THERAPY IN PATIENTS WITH TREATMENT-RESISTANT EPILEPSY
E. Kkolou1, A. Dietsis2, A. Florentzou1, A. Malikkidou1, M. Petsa3, G. Stylianidou1, S. Papacostas1
1Clinical Department, The Cyprus Institute of Neurology and Genetics, 2Neurosurgery Department, 3Neurology Department, Nicosia General Hospital, Nicosia, ‘Neurology Department, Limassol General Hospital, Limassol, ‘Paediatric Neurology Department, Arch. Makarios III Hospital, Nicosia, Cyprus

Background and aims: To investigate the efficacy and tolerability of Levetiracetam (LEV) as add-on therapy in patients with treatment-resistant seizures.

Methods: 65 patients with either focal-onset (75.5%), generalized (18.4%) or unknown etiology (6.1%) of seizures, ages 7–64, were studied retrospectively for 12 months. Patients received LEV as add-on therapy to 1–5 anticonvulsants. We compared mean seizure frequency for a 3-month period prior to and 12 months after introduction of LEV. All subjects had physical and neurological examinations, routine baseline haematological, biochemical, and urinary investigations at entry.

Results: 13 patients (20%) became seizure free. Twelve patients (18.4%) had seizure reduction by 75% or greater. Ten patients (15.3%) had seizure reduction by 50% or greater. Six patients (9.27%) had no significant change from baseline and seventeen patients (26.1%) worsened. Levetiracetam was discontinued in thirteen patients (20%). Reasons for discontinuation of LEV were: lack of efficacy (7 patients; 10.7%), adverse events (6 patients; 9.2%) or both (2 patients; 3%). A reduction of 21.1% on the number of concomitant antiepileptics was achieved in the completers group. Headaches (6.1%), dizziness (7.6%), sedation (10.7%), body pain (6.1%) and behavioural/psychiatric side effects (13.8%) were the most frequently reported side effects.

Conclusions: Levetiracetam was effective in our population with 53.8% of our patients experiencing a reduction of 50% or more on their seizure frequency. It was also well tolerated by the majority of our patients.

P2217
NON-CONVULSIVE STATUS EPILEPTICUS: PRESENTATION OF CASES
M. Liik1, Y. Krikmann1, S. Seeman1
1Department of Neurology and Neurosurgery, 2Department of Intensive Care, University of Tartu, Estonia

Introduction: Non-convulsive status epilepticus (NCSE) is difficult to diagnose and treat. NCSE is defined as diminished level of consciousness or other neurologic deficit, epileptiform activity on the EEG and positive response to anticonvulsants in clinical pictures and on the EEG.

Aim: The aim of this study was to determine the etiology, course, treatment and outcome of NCSE.

Methods: Retrospectively all EEG studies in Tartu University Department of Neurology were reviewed and cases with possible NCSE were selected. Additional clinical data were acquired and cases filling the definition criteria were included in the analysis.

Results: There were 7 patients admitted to the hospital in 2 years and were included in the analysis. There were 3 male and 4 female patients, aged 28 to 81 years. 2 patients had previous history of cryptogenic epilepsy, 2 patients had previous cerebral trauma, 2 patients had stroke and one patient had a history of alcohol abuse. 4 patients had a generalized tonic-clonic seizure evolving to NCSE and 3 patients had a focal seizure in the beginning of the status.

Conclusions: Patients with NCSE need intensive care and combination of treatment with AEDs that may improve the outcome.

P2218
ANXIETY AND DEPRESSION IN EPILEPSY
E. Lučev1, M. Tadinac2, I. Lučev3, J. Lučev4
1Neurological Department, General Hospital Novo Mesto, Slovenia, 2Department of Psychology, University of Zagreb, 3Institute for Migration and Ethnic Studies, 4Faculty of Political Science, Zagreb, Croatia

Background: Approximately 0.5% of the European and USA population are diagnosed with epilepsy. The incidence of epilepsy tends to follow a bimodal distribution, in the first and seventh decade of life. Research shows that 30% of patients diagnosed with epilepsy are also depressive, while 27% suffer from anxiety.

Aim: To determine whether psychotherapy can influence the levels of anxiety and depression in patients suffering from epilepsy with tonic-clonic seizures.

Methods: Patients considered for the study were diagnosed with epilepsy with tonic-clonic seizures and underwent CT and EEG scans. The participants with MMSE results lower than 27 were excluded. The levels of depression and anxiety were determined by ZUNG-A and ZUNG-D instruments 3 and 12 months after the start of psychotherapy. The sample consisted of 32 patients, 17 male and 15 female, aged 22 to 65. All patients were receiving appropriate antiepileptic pharmacotherapy and were in adequate psychophysical condition. All testings and therapies were conducted in a similar microclimate and space conditions between 8 and 11 a.m. in the Neurological Department at General Hospital Novo Mesto.

Results: The anxiety and depression levels in the group of patients suffering from epilepsy with tonic-clonic seizures were significantly lower in the second measurement after regular psychotherapy.

Conclusions: Psychotherapy showed a positive effect on the biopsychosocial status of a small group of epileptic patients. The results also suggest a decrease in epileptic seizures in the second point of measurement. These findings indicate a need for a further multicentre research on a larger sample.
P2219
PROGESTERONE THERAPY IN WOMEN WITH CATAMENIAL EPILEPSY
Neurology Clinic, Silesian Medical Academy, Katowice, Poland

Background and purpose: Progestosterone treatment of epilepsy affected by the menstrual cycle had been rare so far. The aim of the study was to evaluate the efficacy of progesterone therapy in women with catamenial epilepsy.

Material and methods: 36 women with catamenial epilepsy aged 20–40 (mean 30.75±6.0) were studied. 15 patients had tonic-clonic seizures, 10 complex partial and secondary generalized, 8 complex partial, 1 simplex partial, 1 simplex partial and secondary generalized and 1 myoclonic. 13 women were treated with carbamazepine (CBZ), 12 with valproic acid (VPA) and 4 with phenytoin (PHT). 5 patients were taking CBZ + PHT, 1 CBZ + VPA and 1 PHT + VPA. Gynecologic examination, analysis of serum concentrations of progesterone were conducted before and after progesterone administration.

Results: Progesterone therapy lasted 3–45 months (average time of treatment 17.7). 1 patient discontinued treatment after three months with even reduced seizure frequency. In 4 patients seizures declined. In 33 patients seizure frequency declined by 59.3%. There was no improvement in 5 patients and 5 of them experienced an increase in seizures. There were no side effects during therapy.

Conclusions: Favourable effect of progesterone therapy in women with catamenial epilepsy could support this way of treatment in refractory seizures.

P2220
THE COMPARISON OF MONOTHERAPY AND POLYTHERAPY IN THE TREATMENT OF EPILEPSY
M.R. Najafi, M. Reissifar
Department of Neurology, Medical School, Alzahra Hospital, Isfahan, Iran

Background: Monotherapy has been the gold standard in treatment of epilepsy for the last 20 years, partly because of the reputation for increased toxicity of polytherapy. Some clinicians prefer polytherapy from the first time of management of new onset seizures because of decrease in next seizure relapses. The aim of this study answers this question: which to prefer, monotherapy or polytherapy?

Methods: This is a prospective, randomized and clinical trial study of patients with new onset idiopathic generalized & focal seizures that were referred to neurology clinics between 2005 and 2006. These 152 adult patients were divided in two groups randomly. The first group received only one drug (monotherapy with carbamazepine) and the second group was treated with two drugs (carbamazepine plus phenobarbital or phenytoin or clonazepam or lamotrigine (as polytherapy)). Seizure frequencies & relapses were followed up for 6 months.

Results: 152 patients included 82 males & 70 females that were distributed in two groups equally. In the monotherapy group, 6.6% and in the polytherapy group 17.2% had seizure relapses that were significant (p=0.038).

Discussion and conclusion: Full dose carbamazepin as monotherapy has low side effects & more symptom-free periods than polytherapy, (93.4% vs. 82.8%).

P2221
DRUG-RESISTANCE IN EPILEPSY AND UNCONTROLLED SEIZURES AFTER CONSUMPTION OF ANTIEPILEPTIC DRUG IN CHILDHOOD
M. Nobahar, A.A. Vafaei, A. Samaei
Faculty of Nursing and Paramedical, Fatemiah Hospital, Semnan University of Medical Sciences, Semnan, Iran

Previous studies indicated that undiagnosed, uncontrolled seizures can lead to learning, behaviour, and social problems. Also antiepileptic drugs can make seizures less frequent or they can help people with epilepsy leading a completely seizure-free life. The aim of this research was to determine drug-resistant epilepsy and uncontrolled seizures after consumption of antiepileptic drugs at childhood. This study has been done as a clinical trial study and demographic data including age, sex, seizure frequency, epilepsy duration, age at seizure onset in children; medication histories were collected in questionnaires and checklists. Also epileptic children were treated with anti-epileptic drugs including carbamazepine, valproate and phenobarbital. The results indicated that mean age was 13 years, 57% female, 27% with a family history of epilepsy and mean duration of drug use was 4 years. Also 34% of them had intractable or uncontrolled seizures. The findings above show that whereas all patients used drugs, some of them had uncontrolled seizures. Therefore it is important to diagnose seizure disorders early and correctly; treatment of those and selection of the appropriate drug for a given individual must be based on understanding of each drug’s pharmacology and risks.

P2222
QUALITY OF LIFE IN JUVENILE MYOCLONIC EPILEPSY (JME) PATIENTS TREATED WITH TOPIRAMATE
A. Oliveros Cid1, A. Oliveros Juste1, I. Perez Lopez-Fraile1, C. Pascual3, M. Gracia-Naya1, M.A. Cid Lopez1
1Servicio de Neurologia, Clinica Quiron Zaragoza, 2Servicio de Neurologia, Policlinica Sagasta, 3Servicio de Neurologia, Hospital Miguel Servet, 4Servicio de Neurofisiologia, Clinica Quiron Zaragoza, Spain

Background and aims: Topiramate (TPM) is an antiepileptic drug with a broad spectrum of action (due to its mechanism of action), and thus is being increasingly considered a “broad spectrum” antiepileptic drug. It has been successfully used in Juvenile Myoclonic Epilepsy (JME). Our purpose is to evaluate quality of life (QoL) in patients with JME under topiramate treatment.

Methods: We evaluated QoL pre- and post-treatment with TPM in 12 patients suffering from JME (age between 14 and 31 years). We included patients under good pharmacological control but with important adverse effects with the previous antiepileptic drug (AED), patients not controlled with the previous AED and patients without previous treatment. We used generic and specific scales to evaluate QoL, including our specific “Global Epilepsy Chart for Epilepsy in Adults” (Ficha Evolutiva Global de Epilepsia en Adultos, FEGEA).

Results: We checked a global improvement in QoL scores in treated patients, except for those with important adverse effects due to TPM treatment. This improvement was achieved in specific and generic scales. FEGEA showed a very good correlation with the most commonly used QoL scales in epilepsy.

Conclusions: TPM achieves a good effect in quality of life in epileptic patients in general. This benefit appears to be achieved not only due to its proven anticonvulsive effect. So considered, particularly in JME it seems to be a positive “therapeutic benefit” with TPM superior to its pure anticonvulsive efficacy.
Purpose: To assess the clinical picture of nocturnal seizures in epileptic by their unusual clinical presentation.

Methods: 21 patients diagnosed with definite epilepsy with nocturnal predominance of seizures were selected. These patients were referred for night videoEEG monitoring because of unknown or unknown origin of paroxysmal nocturnal events.

Results: 21 patients diagnosed with definite epilepsy with nocturnal predominance of seizures were selected. These patients were referred for night videoEEG monitoring because of unknown origin of paroxysmal nocturnal events. Among them, 15 patients (6 men, 9 women) affected by idiopathic generalized epilepsy were followed for at least 8 months following introduction of levetiracetam. Patients were categorized according to syndrome subtype and final treatment schedule. Patients were included after confirmation of the “intention to treat” from the referring physician. An independent physician analyzed records and evolution.

Conclusion: LEV as de novo monotherapy and add-on therapy at doses between 2000 and 4000 mg/day effectively reduces myoclonic seizure frequency in patients with generalized epilepsy. EEG improvement correlated with clinically relevant antiepileptic effect. LEV was also well tolerated.

Purpose: Open-label study to evaluate the effectiveness of topiramate (TPM) in patients with juvenile myoclonic epilepsy (JME).

Objective: Open label study to evaluate the effectiveness of topiramate (TPM) in patients with juvenile myoclonic epilepsy (JME).
P2228

ROLE OF LEVETIRACETAM IN CESSATION OF REFRACTORY STATUS EPILEPTICUS IN A PATIENT WITH LAFORA DISEASE

M. Hashmi1, F. Saleem1, S. Mustafa1, M. Sheerani1, K.A. Siddiqui1
1Department of Neurology, Aga Khan University Hospital, Karachi, Pakistan

Background and aims: Lafora disease is an autosomal recessive PME of teenagers, characterized by progressive mental decline and intractable seizures. Treating Lafora disease remains a great therapeutic challenge. Though Levetiracetam (LEV) has shown efficacy in other epilepsy syndromes, its use in status epilepticus secondary to Lafora disease is not well established.

Methods and results: We report a 16-year-old male, who presented to us with progressive cognitive decline, ataxia, myoclonic & generalized tonic clonic seizures. His seizure frequency increased with passage of time; he also had frequent hospitalization due to status epilepticus, despite treatment with maximum doses of valproate, clonazepam, lamotrigine and topiramate. His axillary skin biopsy confirmed suspicion of Lafora disease. On this presentation, he was admitted with multiple refractory seizures and was started on infusions of midazolam and propofol. Every time we tried to wean him off from these infusions, he developed clinical seizure activity again. On day 12th, he was given a trial of rapidly escalating doses of LEV, to which he responded dramatically. We were able to wean him off intravenous infusions on 1500 mg of LEV and render him seizure free within 48 hours.

Conclusion: We report this case to show efficacy of LEV in the treatment of refractory status epilepticus, as an adjunct therapy in resistant cases of Lafora disease. Although report of a single case does not prove efficacy beyond doubt but it can be helpful in rescuing patients with intractable seizures, especially in rare epilepsy syndromes where randomized trials are not feasible.

P2227

FREQUENCY OF NON-CONVULSIVE STATUS EPILEPTICUS IN PATIENTS WITH IMPAIRED LEVEL OF CONSCIOUSNESS

N. Jamil1, M. Siddiqui1, A. Bano2, A. Malik3, F.S. Khan4, K.A. Siddiqui5
1Department of Neurology, 2Department of Clinical Neurophysiology, Liaquat National Hospital, Karachi, Pakistan

Background: Non-convulsive Status Epilepticus (NCSE) is an under reported, treatable cause of coma and has a variety of clinical and EEG presentations. We wanted to determine the frequency of NCSE in patients with impaired consciousness.

Methods: We retrospectively reviewed all EEGs in patients with an impaired level of consciousness over four years from 2002–2006. Impaired level of consciousness was sub-divided into unconscious and semiconscious states. All EEGs showing continuous epileptiform discharges were included. Findings of all these EEGs were divided into five groups; generalized spikes and wave, generalized sharp and wave, focal spike and wave, focal sharp and wave and periodic lateralized epileptiform discharges (PLEDS).

Results: There were 785 EEGs recorded in patients with impaired level of consciousness. Out of which 56% (n=440) of patients were semiconscious and 44% (n=345) were unconscious. 1.5% of (n=12) patients who were identified with NCSE on EEG, 66.6% (n=8) were unconscious and 33.4% (n=4) were semiconscious. The commonest continuous EEG findings in our patients with NCSE was focal spike and wave seen in 4 (33%), generalized spike and wave in 3 (25%), generalized sharp and wave in 3 (25%), focal sharp and wave in 1 (8.3%) and PLEDs in 1 (8.3%).

Conclusion: NCSE is a treatable entity which can be easily recognized by doing an EEG. Although in our cohort, numbers of patients with NCSE were small, because awareness regarding this treatable cause for impaired level of consciousness is low. We believe that there should be a high index of suspicion of NCSE in intensive care and high dependency care settings and emergent EEGs should be performed.
Conclusions: We found most patients presented with multiple seizures of generalized type responded well to monotherapy. Hypertension was found in a significant percentage of patients. Single most common etiology was stroke, presenting either acute or remote. We hope that our results although representing only a subset of elderly population will be useful in management of this most frequent form of epilepsy.

P2230
VAGUS NERVE STIMULATION FOR MANAGEMENT OF EPILEPSY
A. Singh, K. Dalal
All India Institute of Medical Sciences, New Delhi, India

Purpose: This study aims at managing patients suffering from intractable epilepsy by applying indirect vagus nerve stimulation (indirect VNS) through reflexology.

Method: This is a 3-years randomized two-arm pilot study. The group in arm one is treated with pharmacological drugs, reflexology therapy and indirect VNS. The second arm comprising the control group continues on anti-epileptic drug therapy. Age group 3 yrs to 45 yrs, who had intractable epilepsy for at least 3 yrs, met the inclusion criteria.

Result: A total of 27 patients have been admitted to the study till March 2006. (Sample size of study group =13 and sample size of control group =14). The response of the patients to the therapy depended on good compliance. 80% of the patients showed a positive response with regards to reduction in seizure frequency, duration of ictal phase and improvement in behavioural patterns of patients, at the end of a 4 months monitoring period.

Conclusion: This is an ongoing study and the patients will be monitored for a period of 3 years. Unique response with Indirect VNS reveals the effectiveness of this technique in managing refractory epileptic patients with least side effect and cost, but with similar results as obtained in an expensive procedure of direct vagus nerve stimulation. Hence this complimentary medicine maintains uninterrupted personal and family lives.

P2231
INFLUENCE OF THE NUMBER OF CONCOMITANT AEDS ON THE EFFICACY OF PREGABALIN AS ADD-ON TREATMENT FOR PARTIAL SEIZURES: AN EXPLORATORY ANALYSIS
T. Tomson1, E. Walner1, R. Benabou1, F. Baldinetti1, T. Leon1
1Karolinska Institutet, Stockholm, Sweden, 2Pfizer Global Pharmaceuticals, New York, NY, USA

Objective: To investigate whether number of concomitant AEDs taken by patients influenced the efficacy of pregabalin add-on treatment of partial seizures.

Background: In highly refractory populations, pregabalin demonstrated safety and efficacy as add-on treatment for partial seizures.

Design and methods: Data were pooled from 5 randomized clinical trials (RCTs). Patients received pregabalin 150 (n=185), 300 (n=242), or 600 (n=532) mg/d or placebo (n=507) for 12–20 weeks. All patients must have been currently receiving ≥1 AED and must not have had a 4-week seizure-free period during baseline; 3 required ≥6 seizures during 8-week baseline; 2 required ≥4 seizures during 6-week baseline. Patients were grouped by number of AEDs taken at baseline: 1, 2, or ≥3. Interaction models were employed to explore for differing trends in efficacy across combinations of treatment and AED usage. Seizure reduction and response rates were estimated for each level of AED usage by treatment.

Results: Number of concomitant AEDs for patients receiving (placebo/pregabalin): 1 AED, (26%, 25%); 2 AEDs, (49%, 50%); ≥3 AEDs, (25%, 25%), respectively. Over the double-blind treatment periods, responder rates (≥50% seizure reduction) were: Placebo – 1AED=22%, 2AEDs=12%, ≥3AEDs=7%; pregabalin 150 mg/d – 1AED=20%, 2AEDs=23%, ≥3AEDs=22%; pregabalin 300 mg/d – 1AED=40%, 2AEDs=43%, ≥3AEDs=22%; pregabalin 600 mg/d – 1AED=46%, 2AEDs=46%, ≥3AEDs=47%. Similar trends were observed for seizure reduction. Interaction models indicated nominal statistical significance for the differing trends (p<0.05).

Conclusions and relevance: Pregabalin demonstrated superiority to placebo at every level of AED usage, suggesting pregabalin add-on treatment can be equally successful irrespective of the number of concomitant AEDs. These analyses were funded by Pfizer Inc.

P2232
LONG-TERM RETENTION OF LEVETIRACETAM IN PATIENTS WITH EPILEPSY IN TAIWAN
J.J. Tsai1, Y.C. Chuang2, M.S. Hsih3, D.J. Yen1
1National Cheng Kung University Hospital and Medical College of National Cheng Kung University, Tainan, 2Chang-Gung Memorial Hospital and Chang-Gung Medical College, Kaohsiung, 3Chang-Gung Memorial Hospital and Chang-Gung Medical College, Taipei, 4The Neurological Institute, Veteran’s General Hospital and School of Medicine, Yang-Ming University, Taipei, Taiwan-R.O.C.

Purpose: To investigate long-term retention of patients receiving levetiracetam (LEV) as part of the Taiwanese registration trial; LEV has been recently licensed for use in Taiwan. This is the first study of its long-term use in clinical practice conducted in an Asian population.

Methods: Case record data were collected on all consecutive patients initiated on add-on LEV (January 2001–January 2002 with follow-up until October 2005) at the National Cheng Kung University Hospital (Tainan), Chang-Gung Memorial Hospital (Taipei and Kaohsiung) and Veteran’s General Hospital (Taipei), as part of the LEV registration trial and subsequent compassionate use pre-registration programme. Kaplan-Meier survival analysis was used to estimate LEV retention rates.

Results: 89 patients were included (49 female, 40 male). Most patients had partial epilepsy and >70% were taking ≥2 anti-epileptic drugs prior to the addition of LEV. Median LEV dose was 2000 mg/day. Estimated retention rate at 3 years was 63%, with ≥3 (3/89) patients seizure-free from first dose. At the last follow-up, 17% (15/89) patients had achieved seizure freedom for >6 months, 48% (43/89) had demonstrated ≥50% seizure frequency reduction for >6 months, and 48% (43/89) were still receiving LEV. Patients stopped LEV due to adverse effects (n=7), inefficacy (n=36), or because they lived too far away to access LEV (n=3).

Conclusions: The estimated retention rate of LEV compares favourably with other AEDs used as adjunctive therapy, with seizure freedom and responder rates maintained in many patients during open follow-up. These long-term data are very similar to Western data.

P2233
A NEUROPROTECTIVE ROLE FOR GABAPENTIN IN STAuroSPORINE-INDUCED APOPTOSIS
M.R. Tuineag1, R. Stoica1, B.O. Popescu1
1University of Medicine and Pharmacy “Carol Davila”, 2National Institute for Research and Development “Victor Babes”, Bucharest, Romania
Apoptotic cell death is involved in a large variety of acute and chronic neurological diseases such as stroke, Alzheimer’s disease, Parkinson’s disease, etc. Neuroprotection consists of strategies that may result in salvage or recovery of the damaged neuronal tissue. We investigated whether the novel antiepileptic drug gabapentin (GP) is neuroprotective against staurosporine (STS) induced apoptosis. We also tried to identify the biochemical mechanism of the hypothesized neuroprotection. We used cerebellar granule cell cultures obtained from baby-Wistar rats, 3–5 days of age. The cells were cultured for 4 days in vitro. Detection of apoptotic cells was performed by annexin V – propidium iodide staining. The cellular viability was assessed by a spectrophotometric method measuring the capacity of the cells to reduce thiazolyl blue tetrazolium bromide to formazan crystals. The mechanism of neuroprotection was investigated by saturating the GABA and AMPA receptors with gamma-amino butyric acid (GABA) and AMPA-kainate receptor antagonist 6-nitro-7-sulfamoylbenzo-(f)quinoxaline-2,3-dione (NBQX), respectively. We found that cell viability was significantly higher in cultures treated with STS+GP as compared to cultures treated with STS alone. Also, GABA (2 mM) was able to completely reverse the increase in cell viability determined by GP in STS-treated cells. In contrast NBQX (100 μM) did not affect the neuroprotection conferred by GP. In conclusion GP is neuroprotective against STS-induced apoptosis through a GABA-receptor mediated mechanism. One possible explanation for this finding is that GP and GABA have an antagonizing effect upon voltage gated calcium channels, with GP being an inhibitor and GABA an activator of these channels.

**P2234**

**FOLLOW-UP OF A PATIENT TREATED WITH VAGUS NERVE STIMULATION FOR REFRACTORY STATUS EPILEPTICUS**

K. Vonck1, V. De Herdt1, H. Verhelst1, B. Dermaut1, I. Dewaele1, L. Waterschoot1, E. Carrette1, A. De Jaeger1, R. Van Coster2, D. Van Roost3, P. Boon1

1Reference Center for Refractory Epilepsy, Department of Neurology, 2Department of Paediatric Neurology, 3Intensive Care Unit, 4Department of Neurosurgery, Ghent University Hospital, Ghent, Belgium

**Purpose:** Vagus nerve stimulation (VNS) is a worldwide established treatment for patients with refractory epilepsy. It is a long-term treatment that has shown increasing efficacy in the months following the start of the stimulation. Refractory status epilepticus (SE) is an acute life-threatening condition with high mortality and few treatment options. We report the follow-up of a patient with refractory SE who was successfully treated with VNS.

**Methods:** A 7-year-old girl with a medical history of hemorrhagic infarction with right thalamic and intraventricular bleeding 8 days after birth, developed epilepsy at the age of 13 months. From the age of 6 on, 3 episodes of non-convulsive SE could be controlled with antiepileptic drugs. She presented with a fourth non-convulsive SE, which was refractory to valproate, phenobarbital, diazepam, fenytoin, topiramate. At time of hospital admission, she was taking a combination therapy of valproate, lamotrigine, clonazepam. A vagus nerve stimulator was placed after 11 days of pentothal-induced coma. Stimulation was initiated shortly after implantation and was increased to 1.5 mA in the following 2 days.

**Results:** Three days after VNS implantation, the pentothal-induced coma could successfully be withdrawn and electroencephalography showed normalization. The patient was discharged from hospital 2 weeks later taking a combination of lamotrigine, ethosuximide, valproate, topiramate, clonazepam. After a follow-up of 8 months she is still seizure-free and AEDs have partially been tapered.

**Conclusion:** This case illustrates a potential acute abortive effect with sustained long-term seizure reduction of left VNS in a 7-year-old girl who presented with refractory SE.

**P2235**

**ASSOCIATED EPILEPSY AND MIGRAINE IN ADULTS – CLINICAL CHARACTERISTICS**

S.M. Vujsic

Department of Neurology, Clinical Center of Montenegro, School of Medicine, Podgorica, Montenegro

**Introduction:** The occurrence of epilepsy associated with migraine is so frequent that it cannot be only a coincidence. Common genetic connection of these two disorders has not been found.

**Aim:** To determine the characteristics of associated epilepsy and migraine, temporally connection, possible common etiology and EEG findings.

**Method:** 69 patients with associated epilepsy and headache, out of 211 consecutive, outpatients with epilepsy, were examined. Epileptic seizures and headaches were classified according to ILAE and ICDH/II. A detailed questionnaire was filled in; neurological examination, EEG, CT and MR were performed.

**Results:** 69 (32.7%) out of 211 patients, had associated headache. 31 (44.9%) of these 69 patients had migraine. In a group of 31 patients with epilepsy and migraine, 25 (80.6%) patients had generalized seizures, and focal seizures were observed in 6 (19.4%) patients. 24 (77.4%) out of 31 patients had migraine without aura, 6 (19.4%) patients had migraine with aura and basilar migraine was observed in 1 (3.3%) patient. 16 (51.6%) patients in a group of 31 patients with migraine and epilepsy had interictal migraine. Postictal and interictal migraine were found in 6 (19.4%) patients, 3 (9.6%) patients had postictal migraine and preictal migraine was found in 4 (12.9%) patients.

**Conclusion:** Associated epilepsy and migraine are significantly more frequent in female patients. In half of the patients migraine occurrence was not temporally connected with the onset of epilepsy. Other patients had postictal (2/3) and preictal migraines (1/3).
Results: Number of concomitant AEDs used at study baselines were: unknown (2.1%), 1 (26.4%), 2 (47.3%), 3 (22.3%), >3 (1.9%). A weight increase trend was evident, at 1 month OL treatment. Rate of increase diminished at ≥4 months. Non-parametric curve estimates of weight change at 1, 2, 4, 6, 9, and 12 months, respectively, were 1.5, 2.1, 3.2, 3.9, 4.6, and 5.2 kg for the placebo/de novo patients and 1.1, 1.3, 2.2, 3.0, 2.7, and 2.7 kg for patients with no data beyond year 1.

Conclusions: Rate of weight increase among placebo/de novo patients receiving long-term pregabalin treatment diminished at ≥4 months. The discontinuation rate attributable to weight change as an AE was 1.4%; weight change estimates in discontinuations during the first year indicated little gain after 6 months, suggesting that for most patients, weight change was not a reason for discontinuation.

Study funded by Pfizer, Inc

P2237
EPILEPSY CONTROL IN ADULTS: FACTORS OF MEDICAL TREATMENT FAILURE
R.M. Zaidan
Department of Neurology, KKUH, KSU, Riyadh, Saudi Arabia

Objectives: 1. To study the response to antiepileptic drugs in different types of epilepsy in adults. 2. To determine the most important factors of response failure to antiepileptic drugs

Methods: 310 patients have been included in a prospective study. They have been followed up for a period of 2–10 years. The data in this study have been obtained from the history (predisposing factors to the attacks, compliance), neurophysiology (EEG findings) laboratory (drug levels and imaging results)

Results: The most important factors in failure to control epilepsy were:
1. In relation with: type of epilepsy: partial complex. Aetiology: lesional epilepsy (details will be presented)
2. Sleep deprive, stress and upset were the other important factors “triggering” the attacks

Conclusions: The results point to a group of factors playing an important role in the failure of control of epilepsy that may be minimized if not avoided resulting in a better control of epilepsy and less undesired consequences

P2238
THE RISK FOR POST-STROKE EPILEPSY
M. Zalete1, B. Zvan1, J. Pretnar-Oblak1, J. Kobal1
Department of Neurology, University Medical Centre, Ljubljana, Slovenia

Introduction: Stroke is the most common cause of seizures in the elderly, and seizures are among the most common neurological sequelae of stroke. We studied clinical features of post-stroke epilepsy.

Methods: We included 124 patients with stroke, 55 pts (mean age 67±6.7 y) with post-stroke epilepsy (PS) and 69 pts age matched (mean age 65±7.1 y) without seizures (S) which were included randomly. All of them had CT scan. The NIHSS were compared between the groups. To test differences between the groups Student-t test in Chi-square were used.

Results: The mean interval from stroke onset to seizure presentation in PS group was 8.7±7.1 months (range from 4 months – 1.5 years). Partial seizures with or without secondary generalization were the commonest type of late post-stroke epileptic seizures. We found significantly higher NIHSS score in PS the group compared to the S groups (7.2±5.1 vs. 9.4±5.9; p=0.029). We found more hemorrhagic strokes in the PS group (34.5% vs. 17.4%; p=0.037). Cortical involvement was found in 44.9 of S pts and 63.6% of pts. The difference was significant (p=0.047).

Conclusion: The risk of post-stroke epilepsy is higher for patients with cortical involvement, hemorrhagic stroke and lower NIHSS score.

P2239
VAGUS NERVE STIMULATION (VNS) THERAPY FOR THE TREATMENT OF PATIENTS WITH CAVERNOUS ANGIOMAS AND PHARMACORESISTANT EPILEPSY
P. Zwolinski1, R. Van Woensel1, M. Roszkowski1
1Department of Neurosurgery, Warsaw Memorial Child Hospital, Warsaw, Poland, 2Clinical Department, Cyberonics Europe, Zaventem, Belgium, 3Department of Neurosurgery, Warsaw Memorial Child Hospital, Warsaw, Poland

Cavernous angiomas (cavernomas) are benign vascular malformations which can be found in any region within the central nervous system. Epilepsy is the most frequent manifestation of this malformation. To achieve optimal treatment of patients with cavernous angiomas and epilepsy, both medical and surgical treatments should be considered.

Patients and methods: A retrospective analysis of data from Cyberonics’ International Patient Registry showed 4 patients (3M, 1F) with cavernous angiomas and pharmacoresistant epilepsy who were treated with VNS Therapy. Mean age: 34±12.83 years (median, 31; range, 23–52); mean age at onset: 14.4±8.14 years (median: 11; range, 9–27). All patients had refractory partial epilepsy. The patients had an average of 12 seizures/month before implantation (range, 6–18). Three patients were evaluated for surgery; information of 1 patient was missing. One patient underwent twice cavernoma resection. MRI results were available for two patients showing multiple cavernous angiomas (n=1) and occipital cavernoma (n=1). Mean follow-up was 34±16.42 months (median, 27; range, 23–58). Results: Mean and median seizure reduction: 41.8% and 36.7%, respectively. Two patients had ≥50% seizure reduction; one of them showed ≥90% seizure reduction. One patient had ≤50% seizure reduction and one patient showed no change in seizure frequency. At the last follow-up visit, patients had an average of 5.6 seizures/month (range, 1–9).

Conclusion: VNS Therapy may be an interesting option for patients with pharmacoresistant epilepsy and cavernomas. These results are encouraging and worth of further investigation.

P2240
ANTIEPILEPTIC DRUG THERAPY AMONG PATIENTS WITH IGE AND MYOCLONIC SEIZURES
G. Ganeva1, M. Rasheva2
1Department of Neurology and Epileptology, SBALNP University Hospital, 2Sector Functional Epileptology and Clinical EEG, UMBAL, Sofia, Bulgaria

P2241
FATTY LIVER INDUCED BY KETOGENIC DIET AND ITS RECOVERY IN RATS
J.M. Kim1, H.D. Park1, S.H. Kang1
1Department of Neurology, College of Medicine, Chungnam National University, 2LG Life Science, Daejeon, South Korea
P2242

Abstract cancelled

P2243

DISEMBRIOPLASTIC TUMORS REVEALED BY REFRACTORY EPILEPSY

C.A. Panea, H. Nicolae, D.G. Stefanescu, G. Vulpe, I. Codita, S. Petrescu, M. Grasu
Neurology Department, Elias Emergency University Hospital, Bucharest, Romania

Autonomic nervous system;
Clinical neurophysiology

P2244

FOCAL TMS HAND REPRESENTATION IN THE AWAKE MONKEY

F. Amaya1,2, D. Liebetanz1
1Department of Clinical Neurophysiology, Georg-August University, Göttingen, Germany
2Cognitive Neurosciences Laboratory, German Primate Center, Göttingen, Germany

rTMS- or tDCS-induced neuroplastic changes of cortical excitability may be of therapeutic value in several neuro-psychiatric disorders. However, more potent stimulation paradigms leading to therapeutically relevant, long lasting, after-effects are required. In order to enable the shaping of advanced stimulation protocols without taking human subjects at risk we developed a primate model of transcranial magnetic stimulation. Surface EMG was recorded either from the right abductor pollicis brevis (ABP) or first dorsal interosseous (FDI) muscle. Motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation were recorded in both muscles. The animal was trained to maintain a relaxed EMG-monitored muscle activity during the stimulation procedure. The coil was placed over the left motor cortex and moved according to a grid of 25 cm² with 0.5 cm intersection lines. After a training period of 3 months the monkey was able to tolerate a 2 hours session of 400 TMS-single-pulses. Resting motor thresholds were determined and calculated conventional nerves in the same limb (technique D). The sensitivities of each test were determined and compared.

P2245

FOCAL EPILEPTIFORM ACTIVITY DESCRIBED BY A LARGE COMPUTERISED EEG DATABASE

H. Aurlien1, I.O. Gjerde1, J.H. Aarseth1, B. Karlsen1, H. Skeidsvoll1, N.E. Gilhus1,2
1Section of Clinical Neurophysiology, Department of Neurology, 2Department of Neurology, Haukeland University Hospital, 3Department of Clinical Medicine, University of Bergen, Norway

Objective:
1) To present a system developed for systematisation and categorisation of visual EEG analysis.
2) To study the age-related topography of epileptiform activity.
3) To study the effect of focal epileptiform activity (FEA) in the general cortical brain activity.

Methods:
Frequency and amplitude of the alpha rhythm (AR) and of the general background activity (GBA) were registered. EEG epochs including the electrodes involved were marked and categorised into a hierarchical system with four main groups; Epileptiform pathology, non-epileptiform pathology, normal variants, and extracerebral activity. 1647 of 12,511 recorded patients (13%) had EEGs with FEA. The background activity in these 1647 EEGs was compared with that in normal EEGs from 3268 drug-free out-patient controls.

Results:
FEA localisation was age-related (p<0.0005) except for the temporal region (p=0.22) where FEA was found equally often in the young and the old. The left hemisphere was more prone to FEA (p=0.018). The left-right asymmetry varied with age (p=0.013). FEA asymmetry occurred most frequently in EEGs from patients older than 80 years, and least frequently in the age-group 20-39 years. FEA was associated with lower AR frequencies (p=0.0041) and higher AR amplitudes (p=0.0023), as well as higher GBA amplitudes (p<0.0005), while GBA frequencies were the same (p=0.96).

Conclusions:
Topographical localisation of FEA was age-dependent. There was an overall left dominance. The side asymmetry was modest and varied by age. FEA was associated with changes in AR and GBA. Storing EEG-descriptions in a categorised database enables studies handling large amounts of data.

P2246

NEW EVIDENCE-BASED ELECTRODIAGNOSIS OF CARPAL TUNNEL SYNDROME

M.H. Chang
Section of Neurology, Taichung Veterans General Hospital, Taichung, Taiwan-R.O.C.

Objective:
To determine which standard techniques recommended by American Academy of Neurology are more appropriate and sensitive for electro diagnosis of carpal tunnel syndrome (CTS)

Methods:
190 suspected CTS patients were recruited and 80 volunteers as controls. We determined and calculated conventional techniques, distal motor and sensory latency (DML and DSL) (technique A); short conduction distance across-wrist for sensory and motor conduction (technique B); comparison of median sensory or motor nerve conduction through carpal tunnel to that of proximal (forearm) or distal segment (digit) (technique C); comparison of median sensory conduction across the wrist with other nerves in the same limb (technique D). The sensitivities of each test were determined and compared.

Results:
Among the 190 CTS patients, 7.9% had normal studies and 92.1% had at least one abnormal electrodiagnostic study. 52.6% had abnormal DML and 66.8% for DSL (technique A). 70% had abnormal wrist-palm motor conduction velocity (WP MCv) and 80% for wrist-palm sensory conduction time (WP SCT) (technique B). 70.5% had abnormal comparison of forearm median motor conduction velocity to W-P MCv (FMVC-WP MCv) and 70% for comparison of W-P SCT to palm to digit conduction time (W-P SCT-P-I SCT) (technique C). 87.4% had abnormal comparison of median to radial conduction time (M-R) and 85.8% for comparison of median to ulnar conduction (M-U) (technique D).

Conclusion:
W-P SCT or M-R or M-U is more sensitive. Technique C is fruitless for an increase of sensitivity.
Results: H-reflex and F-waves were performed. Between 2 and 11 years. Motor and sensory nerve conduction studies. H-reflex and F-waves were performed. Between 2 and 11 years. Motor and sensory nerve conduction studies.

Conclusions: The selective and temporary impairment of H reflex has been confirmed in one of our patients.

Methods: We investigated three paediatric MFS cases, aged 14 years.

Results: Before VD VEP clearly habituated in HV (-13.87±8.99%) but there was, as expected, a potentiation in MO (14.35±15.22%) (p=0.002). In MO this potentiation was replaced by habituation after VD (-3.85±10.05%) (p=0.01) and N1-P1 amplitude in the 1st block decreased significantly (p=0.006). Changes induced by VD were more variable and not significant in HV (1.63±17.63%).

Conclusions: These results suggest that reduced activity of cortical inhibitory interneurons is not responsible for the interictal lack of VEP habituation in migraine or that LD has in migraineurs a paradoxical effect increasing instead of decreasing excitability of these interneurons. Boroojerdi B, Bushara KO, Corwell B et al. Enhanced excitability of the human visual cortex induced by short-term light deprivation. Cereb Cortex 2000;10: 529-534.

Objective: To study the effect of VD on VEP and its habituation in migraineurs without aura (MO) and healthy volunteers (HV).

Methods: Six sequential blocks of 100 averaged VEP at 3.1 Hz were recorded before and after 1 hour of visual deprivation in 6 healthy subjects and in 8 migraineurs. We measured N1-P1 amplitudes in each block and its percentage change between the 1st and the 6th block.

Results: Between VD VEP clearly habituated in HV (-13.87±8.99%) but there was, as expected, a potentiation in MO (14.35±15.22%) (p=0.002). In MO this potentiation was replaced by habituation after VD (-3.85±10.05%) (p=0.01) and N1-P1 amplitude in the 1st block decreased significantly (p=0.006). Changes induced by VD were more variable and not significant in HV (1.63±17.63%).

Conclusions: These results suggest that reduced activity of cortical inhibitory interneurons is not responsible for the interictal lack of VEP habituation in migraine or that LD has in migraineurs a paradoxical effect increasing instead of decreasing excitability of these interneurons. Boroojerdi B, Bushara KO, Corwell B et al. Enhanced excitability of the human visual cortex induced by short-term light deprivation. Cereb Cortex 2000;10: 529-534.

The H-reflex as a diagnostic tool for Miller Fisher syndrome in pediatric patients

B. Dachy1, P. Deltenre1, N. Deconinck1, B. Dan1

1Department of Neurology, ULB, CHU Brugmann, 2Department of Neurology, ULB, HUDEF, Brussels, Belgium

Background: Miller Fisher syndrome (MFS) is characterized by the triad of gait ataxia, external ophthalmoplegia and areflexia. It is considered as an immune disorder involving anti-GQ1b and anti-GT1a antibodies. Immunohistochemical data suggest a direct pathophysiological role for anti-GQ1b antibodies in MFS at motor nerve terminals. The proximal extent of this antibody-mediated degeneration remains uncertain. The variability in abnormal electrophysiological findings reported is important, ranging from isolated H-reflex abolition to widespread nerve conduction impairments.

Methods: We investigated three paediatric MFS cases, aged 2 to 11 years. Motor and sensory nerve conduction studies, H-reflex and F-waves were performed.

Results: All three patients had an absence of H reflex. It was the sole abnormality in two patients whereas the third case had more extended nerve conduction impairments concerning motor and sensory fibres. The transient character of this isolated abolition has been confirmed in one of our patients.

Conclusions: The selective and temporary impairment of H reflex observed in our patients, points to a proximal demyelinating process near the dorsal root ganglia. Based on these findings and recent immunohistochemical advances, we discuss the neurophysiology of areflexia and ataxia in MFS. This may involve selective demyelination of Ia spinocerebellar afferent fibres originating in muscle spindles. H reflex can be proposed systematically as a useful tool in the diagnostic approach of MFS, particularly in a paediatric population in which extensive neurophysiological testing would seem irrelevant.

Cardiovascular autonomic function tests in migraine patients

M. De Marinis, S. D’Arcangelo, A. Petrelli, G. Giannino

Department of Neurological Sciences, La Sapienza University, Rome, Italy

Autonomic nervous system is involved in migraine during (nausea, vomiting, etc.) and outside of the attacks. Most studies, carried out on pupillary autonomic function, have revealed oculosympathetic impairment in migraine patients studied when headache-free. Cardiovascular autonomic function tests have also been studied in migraine patients with different methods and contradictory results. The aim of this study was to assess cardiovascular sympathetic and parasympathetic functions with standardised cardiovascular autonomic function tests in patients suffering from migraine. We studied 30 headache-free patients suffering from migraine (diagnosed according to the criteria of IHS 2004) and 30 age- and sex-matched controls. In these subjects, the following cardiovascular autonomic function tests were performed to assess sympathetic and parasympathetic functions: orthostatism, head-up tilt, cold pressor test, deep breathing, Valsalva manoeuvre and hyperventilation. Blood pressure was globally lower in patients than in controls (p<0.01). In addition, a mild postural hypotension (blood pressure drop >20 mmHg – resulting in a systolic blood pressure <90 mmHg) was found in a subgroup of migraine patients (10/30–33.3%). The responses to deep breathing, Valsalva manoeuvre and hyperventilation were significantly higher in patients (p<0.001) than in controls; an observation that indicates parasympathetic hyperfunction in migraine patients. The possible relevance of low blood pressure, postural hypotension and parasympathetic hyperfunction in migraine patients has to be elucidated in further studies.

Bsi versus the eye: EEG monitoring in carotid endarterectomy

W.A. Hofstra1, M.J.A.M. van Putten2

1Department of Neurology and Clinical Neurophysiology, Medisch Spectrum Twente, 2Institute of Technical Medicine, Faculty of Science and Technology and Biomedical Signals and Systems Group, Faculty of Electrical Engineering, Mathematics and Computer Science, University of Twente, Enschede, The Netherlands

Objective: Carotid endarterectomy is a common procedure as an important secondary prevention of stroke. For selective shunting, continuous EEG monitoring is a standard technique, with visual assessment to track possible ischemia. Recently, the extended BSI was proposed as a pair of quantitative features to support the visual interpretation. Here, we further evaluate its potential clinical use using a large data set.

Method: The extended BSI (consisting of a spatial and temporal symmetry measure, sBSI and tBSI, respectively) was calculated.
P2251
PANIC DISORDERS IN ADULT CELIAC DISEASE
S.V. Kopishinskaya1, A.V. Gustov1, A.A. Repin1, R.B. Medvedev1
1Department of Neurology, Nizhny Novgorod Medical Academy, Nizhny Novgorod, Russia

Background and aims: Celiac disease is an autoimmune gastrointestinal disorder characterized by mucosal atrophy of the jejunum on exposure to gluten, a protein found in grains. An increased prevalence of celiac disease has been reported in psychotic symptoms and depression. We planned to evaluate the association between celiac disease and panic disorders and what part autoimmune impairment of the thyroid may play in it.

Methods: We revealed 28 celiac patients with panic disorders, 21 females and 6 males, aged 16-61. The diagnosis of celiac disease was made on the basis of clinical history, serological criteria and endoscopic duodenal biopsy. Panic disorder was formulated using the International Composite Diagnostic Interview, according to DSM-IV criteria. The thyroid was evaluated with palpation, echography and measurement of serum-free thyroid hormones (FT4, FT3), thyroid-stimulating hormone (TSH) and antithyroid autoantibodies (anti-TPO). Celiac patients were evaluated for the level of knowledge about celiac disease and the compliance with gluten-free diet.

Results: Anti-TPO was significantly high in 17 celiac patients. In 22 patients, the panic disorders improved quickly with a gluten-free diet.

Conclusions: We think celiac disease should be taken into consideration in the presence of panic disorders, particularly if they are not responsive to psychopharmacological therapy, because withdrawal of gluten from the diet usually results in disappearance of symptoms. Screening for celiac disease in all cases of panic disorders with subclinical thyroid disease is therefore recommended.

P2252
RELATIONSHIP BETWEEN ENDOTHELIAL DYSFUNCTION AND VEGETATIVE BALANCE IN PATIENTS WITH HYPERTENSION
U. Rushentsova
Department of Cardiology, Research Centre of Cardiology, Nizhny Novgorod, Russia

Background: We investigated relationship between the endothelium-dependent vasodilatation and the autonomic regulation in hypertensive patients.

Results: All unilateral changes in the EEG found by visual assessment were reflected by Δ-sBSI ≥0.060 and all diffuse changes by Δ-tBSI ≥0.065. In EEGs with both unilateral and diffuse changes, Δ-sBSI ≥0.060 and Δ-tBSI ≥0.065.

Conclusions: This study extends and confirms our previous pilot results that the sBSI and tBSI correlate strongly with the visual assessment of the EEG, as performed by experienced neurophysiologists.

Significance: The extended BSI supports the visual intraoperative EEG monitoring during carotid endarterectomies and assists in a more reliable decision for selective shunting.

P2253
CONTINUOUS EEG MONITORING IN THE INTENSIVE CARE UNIT: BETA SCIENTIFIC AND MANAGEMENT SCIENTIFIC ASPECTS
P. Sanders1, 2, M. van Putten1, 3, N. Maurits1, 4
1Department of Medical Biology, University of Groningen, Groningen, the Netherlands
2Department of Clinical Neurophysiology, Medisch Spectrum Twente, Enschede, the Netherlands
3Department of Neurology, University Medical Center Groningen, Groningen, the Netherlands

EEG monitoring provides a non-invasive and inexpensive method to assess important aspects of the neurologic status of a patient. Because this technique offers an opportunity for long-term brain monitoring, even when patients are comatose or sedated, it can be of great use in the ICU. However, there are various practical and logistical problems that have to be overcome before continuous EEG monitoring (cEEG) can be implemented in the ICU.

In this study, we analyze the aspects that are involved in implementation and use of cEEG in the ICU. The beta scientific aspects that are analyzed are the relevant patient groups that can be monitored and the suitability of the different qEEG features, including automated signalling. The management scientific aspects that are determined are the costs and labour intensity. In this study, we analyze the aspects that are involved in implementation and use of cEEG in the ICU. The beta scientific aspects that are analyzed are the relevant patient groups that can be monitored and the suitability of the different qEEG features, including automated signalling. The management scientific aspects that are determined are the costs and labour intensity.
P2254

EEG FINDINGS IN POST-STROKE SEIZURES: AN OBSERVATIONAL STUDY

U. Yaqub1, M. Siddiqui2, A. Bano1, A. Malik1, F.S. Khan1, K.A. Siddiqui1
1Department of Neurology, Liaquat National Hospital, Karachi, Pakistan, 2Department of Clinical Neurophysiology, Liaquat National Hospital, Karachi, Pakistan

Background: We conducted an observational study in a tertiary referral centre to describe different EEG findings in patients who developed seizures after stroke.

Methods: We reviewed all EEGs that were performed for evaluation of seizures after stroke over one year. We retrospectively recorded demographic data, side of stroke, type of seizures and EEG findings.

Results: A total of 41 patients with post stroke seizures had EEGs done at our laboratory which were reviewed and analyzed. Of these patients, 51.2% (n=21) were males (mean age 60.7; range 22–84 years) and 48.8% (n=20) were females (mean age 63; range 3–90 years). The commonest seizure semiology was focal seizure in 41.5% (n=17) patients, 17.1% (n=7) of patients had normal EEG. Other abnormalities found were focal slowing in 19.5% (n=8), focal sharp and slow waves in 9.8% (n=4), focal spikes & slow waves in 4.9% (n=2), focal sharp waves in 4.9% (n=2) of the patients. Focal spike waves in 2.4% (n=1) and PLEDs were seen in 2.4% (n=1) of patients. 17.1% (n=7) of patients had normal EEG.

Conclusion: Post-stroke seizures are a common entity particularly in the elderly. Generalized seizures and generalized slowing on EEG are the commonest findings in our patients who develop seizures after stroke. The commonest epileptiform discharges were focal sharp and slow waves seen in 9.8% of patients with post stroke seizures.

P2255

THE COLORFUL BRAIN: COMPACT VISUALISATION OF CLINICAL EEG

M.J.A.M. Van Putten
Department of Neurology and Clinical Neurophysiology, Medisch Spectrum Twente, Enschede, The Netherlands

Background: We present a method to transform routine clinical EEG recordings to an alternative visual domain. The method supports the classical visual interpretation and facilitates communication about relevant EEG characteristics.

Methods: EEG features comprise colour-coded time-frequency representations of two novel symmetry measures and a synchronization measure, based on a coherence estimate. This triplet captures three highly relevant aspects of the dynamics of the EEG background pattern. It visualizes the spatio-temporal distribution of the EEG power in the anterior-posterior and lateral direction, and short-distance coherence.

Results: The potential clinical utility is illustrated by application to various EEGs, including seizure activity and the transition to sleep. A transformation of a normal EEG recording is presented in the figure.

Conclusions: Quantitative analysis of clinical EEG to alternative domains assists in the interpretation and contributes to an objective interpretation.

P2256

COMPARISON OF STIMULATED SKIN WRINKLING WITH INTRAEPIDERMAL NERVE FIBRE DENSITY AND NERVE CONDUCTION PARAMETERS IN PATIENTS WITH POLYNEUROPATHY

E.P. Wilder-Smith1, T. Aravinda Kannan1, A. Chow1
1Department of Neurology, National University, 2Department of Neurology, National University Hospital, Singapore

Background: EMLA induced stimulated skin wrinkling (SSW) is a function of small nerve fibre delayed vasoconstriction. Little is known about the relation of SSW with intraepidermal nerve fibre density (IENFD) and other nerve function tests.

Aim: To the study correlation of two measures of small fibre function, SSW and intraepidermal nerve fibre density (IENFD) with parameters of nerve conduction and monofilament testing in polyneuropathy.

Methods: Patients with clinical diagnosis of polyneuropathy were prospectively recruited at the National University Hospital, Singapore. Inclusion criteria was a clinical diagnosis of polyneuropathy. Standardised SSW of digit-5 was performed and graded (scale from 0–4). IENFD was obtained from hypothenar skin using PGP 9.5 immunohistochemistry. Monofilament and nerve conduction was performed for the ulnar and sural nerve.

Results: Tests were performed in 78 patients (mean age 56 yrs, range 20–88). Neuropathy etiology included diabetes mellitus, renal failure, alcohol, idiopathic small nerve fibre disease, and acute inflammatory polyneuritis. Pearson correlation between IENFD and stimulated digit-5 skin wrinkling was significant (p=0.012; r=0.3) as was correlation between IENFD and sural nerve amplitude (p=0.05; r=0.32). All other correlations were not significant.

Conclusions: Two small nerve fibre tests, SSW and IENFD show statistically significant correlation in patients with polyneuropathy from a variety of causes. Correlation of SSW with sural nerve amplitude is likely a result of the latter being a sensitive marker of sensory neuropathy which depends on the underlying etiology and frequently involves both small and large fibres.

P2257

AUTONOMIC DYSFUNCTION IN ISAACS SYNDROME: A CASE WITH ASYMMETRICAL SYMPATHETIC STIMULATION

M. Yoshioka1, H. Onodera1, H. Saito2, T. Takahashi1, H. Kommo1, H. Tanaka1, M. Endo1
1Department of Neurology, National Hospital Organization Nishitaga Hospital, 2Department of Neurology, Sendai-Higashi Neurosurgical Hospital, 3Department of Neurology, Tohoku Kouseinenkin Hospital, Sendai, Miyagi, Japan
Background and aims: Autonomic dysfunction in Isaac’s syndrome has not been documented in detail so far. We now describe a case of Isaac’s syndrome with positive voltage-gated potassium channel (VGKC) antibody in the serum, who presented clinical features of reflex sympathetic dystrophy.

Methods: A case report including electrophysiological studies and autonomic function tests.

Results: A 55-year-old male developed pain and weakness in the right lower limb and subsequently in the right upper limb during 10 months. On examination pupils and palpebral fissures were larger on the right side. Painful right limb were stiff with normal deep tendon reflexes. Muscle weakness, contractures, swelling and trophic change of the skin with dark discoloration were also observed. Thermogram showed lower skin temperature in the right side of the body. Thermal sweat test showed a dominant sweating on the right side. Electromyogram revealed spontaneous muscle fibre activity (doublets discharges). Nerve conduction studies were normal. Serum VGKC antibody was positive in high titre; thus diagnosis of Isaac’s syndrome was made. In addition, hyperalgesia, low skin temperature, sweating change, and trophic changes of skin in the affected limbs were consistent with complex regional pain syndrome type I (reflex sympathetic dystrophy). Limited relief of painful neuromyotonia was obtained by plasmapheresis.

Conclusions: The present case suggests that autonomic involvement of Isaac’s syndrome may be due to direct effects of VGKC antibody to sympathetic nerve fibres, and that asymmetrical or localized manifestations may be due to interactions between sympathetic outflow and somatic afferent fibres stimulated by painful neuromyotonia.

P2258

ACUTE LOWER MOTOR NEURON FACIAL PALSY: CLINICAL AND QUANTITATIVE ELECTROMYOGRAPHIC (QEMG) PREDICTIVE VALUE

F.A. Abd Allah1, N.Z. El Shazle1, N.M. Shalbe1, H.A. Shaheen1, E.S. Bellal1

1Neurology Department, 2Clinical Neurophysiology Department, Cairo University Hospital, Cairo, 3Neurology Department, El Fayoum University Hospital, Fayoum, Egypt

Aim of work: This study was designated to determine the value of short-term clinical monitoring and the role of the newly emerging quantitative electromyography (QEMG) as predictors of the outcome of acute lower motor neuron facial palsy.

Patients and methods: A total of 40 patients with acute idiopathic lower motor neuron facial palsy were recruited and 40 healthy volunteers as a control group. The House-Brackmann facial nerve grading system was used to clinically grade the degree of facial palsy in all patients. QEMG of the orbicularis oculi muscle can be helpful in predicting the prognosis in cases of idiopathic LMN facial palsy.

Conclusions: Clinical factors and QEMG of the orbicularis oculi muscle can be helpful in predicting the prognosis in cases of idiopathic LMN facial palsy.

P2259

PSYCHOSOMATIC ASPECTS OF HYPERTENSION: CARDIAC AUTONOMIC DYSFUNCTION AND ANXIETY

Z. Bajko1, K. Csapo2, S. Molnar2, T.M. Magyar2, E. Nyitrai3, P. Soltesz4, L. Csiba2

1Department of Neurology, Mures County Emergency Clinical Hospital, Targu Mures, Romania, 2Department of Neurology, Medical University of Debrecen, 3Institute of Psychology, University of Debrecen, 4Department of Internal Medicine III, Medical University of Debrecen, Hungary

Background: Numerous studies indicate a relation between chronic mental stress and atherosclerosis, thrombosis, and sudden death. Autonomic dysregulation is present in the early stage of hypertension. The aim of this study was to investigate the relationship between cardiac autonomic dysfunction and anxiety.

Methods: 28 recently diagnosed, untreated hypertensives and 28 healthy volunteers were examined. We investigated the cardiac autonomic dysfunction with complex haemodynamic monitor during tilt table examination. From the simultaneously recorded EKG and beat to beat blood pressure signal, the special software of the monitor performed the power spectral analysis of heart rate and blood pressure variability. Vagal tone is represented by the high frequency band of HRV, sympathetic tone by the low frequency band. The anxiety was assessed with Spielberger State questionnaire.

Results: The Spielberger test indicated significantly higher anxiety score in hypertensives (p=0.048). The LF-component of HRV (LF-RRI) was significantly lower in hypertensives during passive orthonostasis. The LF-RRI decreased in orthonostasis in the hypertension group, and increased in the control group. In the hypertension group the sympathetic activity was significantly higher in both in lying and orthonostatic position. The LF/HF-ratio of HRV was also significantly higher in males. We find significant negative correlation between the Spielberger score and the difference between „LF-component” of HRV in lying and passive orthonostatic position (Spearman r=−0.527).

Conclusions: There is an important psychosomatic component in the pathogenesis of hypertension. The analysis of heart rate variability indicates important cardiac autonomic dysfunction in recently diagnosed hypertensives. The gender differences in heart rate variability in hypertension can explain the higher cardiovascular risk in males.

P2260

LOW FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION OF THE SENSITIVE CORTEX MODIFIES SPATIAL DISCRIMINATION THRESHOLD OF PAIN IN THE TRIGEMINAL AREA

C.R. Bohotin1, V. Bohotin1, C. Meriuta1, O.C. Mungiu1, D.F. Muresanu1, C.D. Popescu2

1Center for Study and Therapy of Pain, Laboratory of Neurology and Neurobiology, 2Department of Neurology, University of Medicine and Pharmacy, Iasi, 3Department of Neurology, University of Medicine and Pharmacy, Cluj-Napoca, Romania

Background: Recent studies demonstrate that transcranial magnetic stimulation (TMS) has direct effects on sensory thresh-
old for cold and heat (Johnson et al. 2006) and prick pain (Porro et al. 2007), when applied on motor (20 Hz) respectively parietal cortex (25 Hz).

**Aim:** To modulate the spatial discrimination threshold for pain in the trigeminal area by using rTMS.

**Methods:** The study was performed on 11 healthy right-handed volunteers, without diseases which modify cortical excitability. The painful spatial discrimination of the upper lip was determined with a compass-like instrument before and after rTMS (1 and 5 minutes after stimulation, respectively). The painful discrimination has been done symmetrically on the right and left upper lip, respectively. The rTMS was applied on the sensitive cortex, using the following parameters: intensity 110% from the motor threshold, frequency 1 Hz, time 200 seconds.

**Results:** The 1 Hz rTMS determines a significant increase (p=0.03) of spatial discrimination threshold from 4.6±1.5 mm before, to 7.8±3.1 mm (1 minute after stimulation) and 7.2±2.9 mm (5 minutes after stimulation) in the half right, respectively. On the left half of the lip there were no significant modifications (p=0.09) after rTMS.

**Conclusions:** Our study demonstrates that 1 Hz rTMS of the sensitive cortex can modulate the tactile discrimination in the trigeminal area (maxillary branch of the trigeminal nerve). The inhibitory effect supports the idea that the postcentral gyrus from the parietal lobe is the main site of trigeminal pain integration and inhibitory effect supports the idea that the postcentral gyrus from the parietal lobe is the main site of trigeminal pain integration. The painful discrimination has been done symmetrically on the right and left upper lip, respectively. The rTMS was applied on the sensitive cortex, using the following parameters: intensity 110% from the motor threshold, frequency 1 Hz, time 200 seconds.

**Methods:** The study was performed on 11 healthy right-handed volunteers, without diseases which modify cortical excitability. The painful spatial discrimination of the upper lip was determined with a compass-like instrument before and after rTMS (1 and 5 minutes after stimulation, respectively). The painful discrimination has been done symmetrically on the right and left upper lip, respectively. The rTMS was applied on the sensitive cortex, using the following parameters: intensity 110% from the motor threshold, frequency 1 Hz, time 200 seconds.

**Results:** The 1 Hz rTMS determines a significant increase (p=0.03) of spatial discrimination threshold from 4.6±1.5 mm before, to 7.8±3.1 mm (1 minute after stimulation) and 7.2±2.9 mm (5 minutes after stimulation) in the half right, respectively. On the left half of the lip there were no significant modifications (p=0.09) after rTMS.

**Conclusions:** Our study demonstrates that 1 Hz rTMS of the sensitive cortex can modulate the tactile discrimination in the trigeminal area (maxillary branch of the trigeminal nerve). The inhibitory effect supports the idea that the postcentral gyrus from the parietal lobe is the main site of trigeminal pain integration and offers the premises of using the rTMS for trigeminal pain treatment.
myorelaxation of muscles participating in dystonia, we revealed normalization of alpha-rhythm parameters and its zonal distribution.

**Conclusions:** Spasmodic torticollis patients had a temporary weakening of dystonia manifestations during correcting gestures and also after injection of BtxA accompanied with normalization of essential rhythms parameters in EEG registration. This can also suggest the distortion of bioelectric activity of the brain in standard conditions of EEG records due to significant muscle tension.

**P2264**

**CARDIAC AUTONOMIC DYSFUNCTION IN HYPERTENSIVE PATIENTS**

K. Csapo1, Z. Bajko1, S. Molnar1, M.T. Magyar1, P. Soltesz1, L. Csiba1

1Neurology Department, University of Debrecen, Hungary, 2Neurology Department, University of Tirga Mures, Romania, 33rd Internal Medicine Department, University of Debrecen, Hungary

The dysregulation of the autonomic nervous system plays an important role in the development of hypertension. The heart rate variability and baroreflex sensitivity are established methods for the evaluation of the cardiac autonomic activity and provide the assessment of the sympathetic and vagal activity. Our purpose is to measure the cardiac parameters of the autonomic nervous system in hypertensive patients and the efficacy of the antihypertensive treatment by a non-invasive technique. Heart rate variability calculated with spectral analysis and baroreflex sensitivity obtained by the sequence technique were measured in 28 healthy persons (age: 48.29±8.14 yrs, m/f rate: 1) and 28 hypertensive patients (age: 46.1±6.54 yrs, m/f rate: 1:1) by Task Force Monitor during head-up tilt table test. The number of the baroreflex sequences was significantly higher (66.9 vs. 51.1; p=0.031), the baroreflex effectiveness index was significantly lower (67.3 vs. 58; p=0.027) in the hypertensive group. Also significantly lower heart rate variability was measured in the low frequency (LF-RRI) range (213 ms² vs. 468.2 ms²; p=0.018) in the hypertensive group. The decreased baroreflex sensitivity and heart rate variability proved the autonomic dysfunction, the lower sympathetic activity indicated long-standing systemic hypertension in the hypertensive group.

**P2265**

**PROGNOSIS VALUE OF SOME NEUROPHYSIOLOGICAL METHODS OF RESEARCH IN CEREBRAL STROKE**

B.G. Galurov, N.A. Alikulova

Medical Refresher Institute, Tashkent, Uzbekistan

Working out objective and accessible methods of non-invasive research with acute stroke, is of great importance. We have investigated the prognosis value of such methods as electrophysiological analysis of orienting reflex, EMG-analysis of winking reflex and bilateral analysis of galvanic skin reflex from extremities. 69 patients with hemispheric ischemic stroke were examined. The research with the use of above-mentioned methods was taken in the dynamic from first hours after the stroke up to the third week after the stroke.

Analysis of the orienting reflex has shown that its absence during up to the end of the first week, of the basic electrophysiological indicators (vertex – potential, EEG reaction – desynchronization and skin galvanic reflex) in response to sound stimulation is an unfavourable sign of vital prognosis. Presence of all the components of the orienting reflex and their quick recovery in the dynamic, is a favourable prognosis sign.

Analysis of winking reflex with the use of stimulation EEG has shown that gross disorder and especially absence of all the components of winking reflex is an indicator of unfavourable clinical and vital prognosis. Undamaged state of late components of winking reflex from the ipsilateral side is informative in terms of making prognosis of possibility for recovery of lost functions. The research of skin galvanic reflex has established that reduction of intensity of stimulated skin galvanic reflex (response to a sudden sound stimulation) in paralyzed extremities in more than 30% compared to undamaged side, proves the stabilities of hemiparesis.

**P2266**

**CLINICAL APPROACH BY TESTS TO THE SEVERITY OF CARPAL TUNNEL SYNDROME IN COMPARISON WITH NEUROPHYSIOLOGICAL PARAMETERS**

G. Garcia-Martin1, M.S. Dawid-Milner2, M. Romero-Acebal1, M.I. Chamorro-Muñoz1, F. Perez-Errozain1

1Neurology Department, Virgen de la Victoria Hospital, 2Human Physiology Department, Facultad de Medicina, Universidad de Malaga, Spain

**Introduction:** Carpal tunnel syndrome is a pressure-induced neuropathy that causes sensorimotor disturbances of the median nerve which impair functional ability. It is known that the diagnosis is not so easy nowadays. There are discrepancies on the value of specific symptoms and clinical tests. Lots of studies have been carried out in order to validate these tests and to measure the changes to the result of these tests after treatment. Apart from the clinical diagnosis and the tests there is an electrodagnosis but it may not detect transient or mild carpal tunnel syndrome.

**Objectives:** To make a clinical approach to the severity of carpal tunnel syndrome without electrodagnosis presenting the relation between the results of two questionnaires, DASH and CTS, and neurophysiological parameter.

**Methods:** 48 patients. We asked them two questionnaires validated in Spanish by Rosales et al: DASH (disabilities of hand, shoulder and arm) and CTS (carpal tunnel syndrome). We carry out the electrodagnosis. We compared both results.

**Results:** We find a statistic correlation between the results of both tests and neurophysiological parameters so that we distinguished the most severe cases from the mildest ones through the questionnaires.

**Conclusions:** Although electrodagnosis is necessary in most of the cases of carpal tunnel syndrome to decide treatment, we think it is possible to approach the severity of each case using DASH and CTS questionnaires. This could let us anticipate the electrodagnostic test and treatment in several ones to improve clinical attendance.

**P2267**

**DOES IMPOSED MECHANICAL MOTION AT HIGH FREQUENCIES INFLUENCE HIGH FREQUENCY OSCILLATIONS IN CONTROLATERAL PHYSILOGICAL HAND TREMOR?**

G. Grimaldi1, L. Sattar2, P. Lammertse1, M. Manto1

1Department of Neurology, AUOP, Palermo, Italy, 2Neurologie, ULB, Brussels, Belgium, 3‘FCS Schiphol. The Netherlands

**Background:** Addition of inertia, ischaemic nerve block, fatigue, and cognitive tasks are known to induce modifications in tremor frequencies in upper limbs. Tapping test may also affect tremor features in contralateral limb.

**Objective:** To test the hypothesis that superimposed motion at high frequencies in one upper limb influences contralateral postural physiological tremor.
Methods: we recorded the postural physiological tremor in both right and left hands during an outstretched upper limbs condition (basal condition) in 7 control subjects (mean age: 50.1±16.5 years; sex: 4F/3M). We analysed right hand while subjects were performing a tapping task with the contralateral limb at different frequencies. We studied the effects of imposed movements at high frequencies (13.3 Hz; 15 degrees) of right hand on left upper limb postural tremor using a myohaptic device (wristalyzer). Spectral analysis of the tremor was evaluated with Fast Fourier Transform. Integrals of the bands 20–100 Hz were calculated under these different conditions.

Results: basal values for the integrals 20–100 Hz for the right hand were 0.0016±0.0011. During the tapping test, integrals were 0.0013±0.0005 a.u. (0.5 Hz), 0.0014±0.0005 a.u. (1 Hz) and 0.0014±0.0006 a.u. (2 Hz) (p=0.598, p=0.727, p=1), respectively. During high frequency imposed motion, integrals were 0.0017±0.0008 a.u. and 0.0017±0.0005 a.u., respectively, in basal condition and with imposed motion (p=0.456).

Conclusion: High frequency oscillations during postural physiological tremor are poorly influenced by high frequency imposed motion. Modulation of high frequency spectral signals related to motoneuronal commands is not directly sensitive to high frequency discharges resulting from proprioceptive inputs in contralateral upper limb.

P2268
ARE ELECTROMAGNETIC FIELDS ON WITHDRAWAL SYNDROME A SIGN OF MORPHINE?

H. Jafari, A. Safari, M. Shahidi
Department of Pharmacology, Department of Occupational Health, Qazvin Medical University, Qazvin. Department of Haematology, Iran Medical University, Tehran, Iran

Background: many studies have been shown that electromagnetic field decreases WSSM.

Objectives: Effect of electromagnetic field on WSSM investigated in rats.

Materials and methods: In this study 102 male rats with weight about 225gr were classified in 17 groups (n=6). They were addicted to morphine by injection according to Pinelli Method.16 groups of them were exposed to electromagnetic field with 2.5, 50, 75 and 100 Hz frequency and with magnetic field 0.5, 1.5, 2.5 and 3.5 G intensity. One group was chosen as control. WSSM jumping, climbing, rearing, diarhhea, weight loss, ptosis and yawning by naloxone injection in pretoon (5 mg/kg) on all animals were investigated.

Findings: WSSM were obtained by counting the jumping, yawing, climbing, rearing and the ptosis, diarhhea were scored from +1 to +4 .Also weight losses were measured in all groups.

Results: This study showed that magnetic field caused the significant decreased on waving, ptosis, weight loss and diarhhea at all of exposure groups (p<0.001). Rearing and climbing decrease significantly in groups that were exposed to electromagnetic fields and these fields with 25 Hz frequency and 0.5 G intensity have minimum and with 100 and 75 Hz frequency 3.5 G intensity have maximum effects on WSSM.

P2269
EEG-MAPPING IS AN INDICATOR OF LONG LASTING RTMS EFFECTS IN ISCHEMIC STROKE PATIENTS

V.V. Kistser, V.V. Evstigneev
Neurology Department, Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus

The objects of this study were the data of EEG-mapping of ischemic stroke patients before and after repetitive transcranial magnetic stimulation (rTMS).

Methods: We performed a study of 112 patients (64 men and 45 women, mean 52.2±9.17 years old) with brain hemispheric infarct in early and late rehabilitation period. rTMS was implemented in basic group using the original method: intensity of magnetic field 1.7 T, frequency 10 Hz, stimulus duration 250-msec. The stimulation coil was applied on projection of stroke localization. The time of magnetic influence of the mentioned parameters was 10 min. The course treatment included from 8 to 10 daily procedures of rTMS. Patients in the control group had traditional rehabilitation without rTMS. EEG-mapping analysis was performed by the computer system «Brainscan» with quickly Fourier transform. The mean and peak frequency of alpha-rhythm, index, focus and regularity of beta-rhythm were evaluated.

Results: All patients had EEG pathologic changes: decreasing of index, regularity, peak frequency of alpha-rhythm against the background increasing beta-rhythm of low amplitude. There were statistically reliable change data in rTMS group (especially in early rehabilitation period) after rehabilitation course. Positive dynamic consisted in increasing frequency inversion of alpha-rhythm in early (p=0.027) and late (p=0.04) rehabilitation period, in decreasing beta-index (p<0.04), beta-regularity (p<0.03) and focusing of beta-rhythm (p<0.035). There were not statistically reliable change data in control group (p>0.05).

Conclusions: 1. rTMS exerted modulated effect on neuronal plasticity of ischemic stroke patients. 2. EEG-mapping – method for registration of long lasting rTMS effects.

P2270
REALIZATION OF THE POSTURE MAINTENANCE ALGORITHM OF HEMISPHERIC STROKE PATIENTS

V.V. Kistser, V.V. Evstigneev
Neurology Department, Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus

The aim of this study was to assess the influence of optic and proprioceptive analyzer to posture maintenance algorithm of hemispheric stroke patients.

Methods: We performed a study of 14 patients (mean age was 48.5 ± 5.73 years) with hemispheric brain infarct in early and late rehabilitation periods. Posture disturbance was objected by posturography in optic and acoustic regimes. Next we used posturography parameters: efficacy of posture retention (EPR), mean time of mistake (MTM), coefficient of optic participation (COP) and index “K” (IK). COP = ((y–x)/x) ·100, x – mean time of mistake in optic regime, y – mean time of mistake in acoustic regime. Positive value of COP interprets as prevalence of optic analyzer function in posture retention algorithm. IK = (MTM2-MTM1)/(ERP2-ERP1), MTM2 and ERP2 – parameters after rehabilitation, MTM1 and ER1 – parameters before rehabilitation. IK is an exponent of stimulus verbalization ability. Positive value of IK interprets as a phenomenon compensation insertion.

Results: We found negative correlation between central conduction time (parameter of somatosensory evoked potentials) and Spielberger-Hanin scale summary point with IK in optic stimulus. These facts confirm the hypothesis of predominance of optic analyzer of hemispheric stroke patients with sensory and anxiety disorders. Positive correlation between P300 latency and COP confirm predominance of optic analyzer of stroke patients with cognitive disorders in proprioceptive analyzer participation descent.
Conclusion: Thus, results received increase the understanding of the mechanism of posture organization and maintenance in pathology and interpret reactions of altered brain.

P2271
NEUROPHYSIOLOGIC DIFFERENTIAL DIAGNOSIS BETWEEN POLYNEUROPATHY WITH ANTI-MAG ANTIBODIES AND CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY
O. Koutoula, K. Papadopoulos, K. Boutsi, I. Mavromatis, N. Taskos
Neurological Department B’’, AHEP University Hospital, Thessaloniki, Greece

Background and aims: There is some controversy concerning the usefulness of the electroneurographic parameters such as distal motor latency (DML), terminal latency index (TLI), or motor conduction velocities for the distinction between chronic inflammatory demyelinating polyneuropathy (CIDP) and anti-myelin-associated-glucoprotein antibodies polyneuropathy (anti-MAGP). Standard electrophysiological testing may not discriminate between CIDP and anti-MAGP. We performed this study in order to search for the best parameter that might help to distinguish anti-MAGP from CIDP.

Methods: We examined 5 patients with an anti-MAGP and 5 patients with a CIDP. The electroneurographic features that were studied: distal compound motor action potential (CMAP), DML, motor conduction velocity (MCV) elbow to wrist (distal MCV), MCV axilla to elbow (proximal MCV), MCV distal/proximal, TLI, residual latency (RL), F-wave, and modified F ratio.

Results: Comparisons between the anti-MAGP and the CIDP groups showed significant differences between the mean DML and RL, but not the mean TLI. The DML has a median of 6 ms in the anti-MAGP and 3.3 ms in the CIDP group. The median of RL is 3.8 in the anti-MAGP group versus 1.8 in the CIDP group. The median of the TLI is 0.38 in the anti-MAGP group versus 0.48 in the CIDP group.

Conclusions: There is no specific biological marker for CIDP in contrast with the anti-MAGP. Electrophysiological testing can be helpful in the distinction between CIDP and anti-MAGP. We propose that a residual latency >4.0 and a distal motor latency >6.5 are suggestive for an anti-MAGP.

P2272
SUPRANUCLEAR PALSY OF VOLUNTARY EYELID CLOSURE: ELECTROPHYSIOLOGICAL CORRELATION
S.B. Kwan1, H.S. Kim1, S. Jung1, S.H. Hwang1
1Department of Neurology, Hallym University College of Medicine, Kangnam Sacred Heart Hospital, 1Department of Neurology, Kangbuk St. Mary’s Hospital, Seoul, South Korea

Background and significance: Supranuclear palsy of voluntary eyelid closure is a motor dysfunction that reflects the inability to close the eyes either willfully or on command, with preservation of reflex blinking. The anatomical and pathophysiological basis of this uncommon motor eyelid dysfunction remains unclear.

Case: A 66-year-old man was presented with non-convulsive status epilepticus. After improvement of status, he showed a complex ophthalmoplegia including saccadic pursuit, hypometric saccades, absence of optokinetic nystagmus, and disturbances of horizontal and supranuclear vertical gaze. In addition, the patient was unable to close the eyes voluntarily or on command, although reflex blinking to glabellar or corneal stimulation was preserved. Frontal cortical perfusion defect was found on SPECT. Coaxial needle electro-myographic recording was obtained simultaneously from levator palpebrae superioris (LPS) and orbicularis oculi (OO) muscles and revealed a combination of inadequate inhibition of LPS and insufficient activation of OO.

Comment: We report a man who showed supranuclear palsy of voluntary eyelid closure. It is suggested that supranuclear palsy of voluntary eyelid closure may be due to a deficit of frontal cortical inhibition of LPS than insufficient OO activation.

P2273
MOTOR CORTICAL EXCITABILITY IN PATIENTS WITH POST-STROKE EPILEPSY
H.W. Lee1, J.H. Kim1, L.G Cohen2, K.D. Park1, K.G. Choi1
1Department of Neurology and Medical Research Institute, College of Medicine, Ewha Womans University, Seoul, South Korea, 2Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic, National Institutes of Neurological Disorders and Stroke, Bethesda, MD, USA

Background and aims: To gain insight into the mechanisms underlying poststroke epilepsy (PSE), we evaluated motor cortical function in chronic stroke patients with (n=18) and without (n=18) PSE.

Methods: We measured resting motor threshold, (RMT), motor evoked potential (MEP) amplitudes, cortical silent period (CSP), intracortical inhibition (ICI), influenced by GABAergic neurotransmission, and intracortical facilitation (ICF), influenced by glutamatergic activity, to transcranial magnetic stimulation (TMS).

Results: We found (1) larger MEP amplitudes and ICF, in the affected than unaffected hemispheres of patients in the PSE group but not in patients without epilepsy, and (2) comparably higher RMT and longer CSP in the absence of differences in ICI, H-reflexes or F-waves in the affected and unaffected hemispheres of both PSE and non-PSE patients.

Conclusions: Our results suggest that different expression of intracortical glutamatergic activity could be one of the mechanisms contributing to the development of poststroke epilepsy.

P2274
ETHNIC DISTRIBUTION OF CARPAL TUNNEL SYNDROME IN SINGAPORE
E. Li1, T. Aravinda Kannan1, Y.C. Chan1, E.P. Wilder-Smith1
1Neurology Diagnostic Laboratory, NUH, 1Department of Neurology, National University Singapore, Singapore, Singapore

Background: Carpal tunnel syndrome (CTS) is the most common cause for referral to our clinical neurophysiology service in Singapore. The role of ethnicity on CTS is currently not known.

Aim: To estimate the ethnic distribution of patients with confirmed neurophysiological CTS in the multicultural society of Singapore.

Methods: This is a retrospective study of all patients referred to the Neurology Diagnostic Laboratory at the National University Hospital, Singapore, for the year 2004. Inclusion criteria were the presence of neurophysiologically verified CTS. Standard neurophysiological criteria demonstrating focal median nerve slowing at the wrist were applied. Ethnic groups included were Chinese, Malay, Indian and other ethnic groups.

Results: 311 patients were retrieved. 234 (75%) were female, mean age was 54 range 20–90. Ethnicity of patients with CTS was: 229 (73%) Chinese, 38 (12%) Malay, 34 (11%) Indian, 10 (3%) from other ethnic groups. According to official statistics, the distribution of ethnic groups in Singapore is: Chinese 77%, Malay 14%, Indian 8%, other groups 1%.
Conclusion: The ethnic distribution of patients with confirmed neurophysiological CTS in the multicultural society of Singapore is similar to that of the general population. This suggests that in our population there is no ethnic predisposition to CTS.

P2275
ATROPINE PREMEDICATION AND THE AUTONOMIC NERVOUS SYSTEM RESPONSE FOLLOWING ELECTROCONVULSIVE THERAPY
M. Mahdian, S. Nourizad, G.H. Mousavi
Anesthesia Department, Beheshti Hospital, Kashan, Isfahan, Iran

Background and aim: Electroconvulsive therapy (ECT) is a useful non-pharmacologic treatment for managing major depression, however, it may lead to bradycardia and maybe consequently to tachycardia and hypertension due to autonomic nervous system response to ECT. Use of atropine as a routine pre-medication to control hemodynamic changes in such patients is controversial. This study was designed to consider the effect of atropine pre-medication on cardiovascular changes during ECT.

Methods: 80 patients entered this double–blinded clinical trial. Patients were randomly assigned to either case or control groups. The case group (n=40) was intravenously given 0.5 mg atropine before the anesthesia induction; however, the control group (n=40) received 1 ml normal saline. Blood pressure and heart rate were monitored 1 minute after the induction, and minutes 1, 3, and 5 after ECT.

Results: The mean age of case and control group was 35.3±7.8 and 33±7.6 years respectively (NS). At minute 3, the mean blood pressure was higher in the case group (p=0.043). At minutes 1 after induction of anesthesia and 5 after ECT the mean heart rate was faster in the case group (p=0.05).

Conclusion: Administration of atropine as a pre-medication agent may lead to transient hypertension and tachycardia, meanwhile, those who have not received atropine (control), had no bradycardia. We suggest atropine as a pre-medication before ECT only in whom hypodynamic heart, usage of sympathetic inhibitor, and previous history of bradycardia following the ECT procedure exist. In other circumstances it maybe used if needed.

P2276
INVERSION OF ANODAL POSITION DURING GVS IN HEALTHY SUBJECTS REVEALS AN OVER-COM pensation BEHAVIOR
L. Sattar, M. Mantu, G. Grimaldi
1Department De Neurologie, Hopital Erasme, ULB, Brussels, Belgium, 2Department of Neurology, AUOP, Palermo, Italy

Background: Galvanic Vestibular Stimulation (GVS) determines balance responses inducing a shift of the sway towards the anodal side, as well as a deviation from the subjective vertical. Many areas are involved in processing vestibular information for head and body orientation in space (supramarginal gyrus, post lateral thalamus, cerebellar vermis, posterior insula and hippocampal regions).

Objective: to study the postural effects of polarity inversion during GVS.

Methods: we analysed the postural behaviour during standing position (eyes open and feet apart) of five healthy subjects (mean of age:22.6±3.05; SF). Lateral sways (Δx), antero-posterior sways (Δy), and the total travelled way (TTW) of the centre of pressure were measured, with a pressure-sensitive calibrated platform. We compared values of three conditions: without GVS (basal condition), under GVS (9 V with 6F22 battery) with the current delivered with an anodal electrode on the right mastoid process (anode right condition), followed by current delivery on the contralateral side.

Results: we found a significant modification between Δx, Δy and TTW of basal and “anode right condition”, with a drop of values. Δx, Δy and TTW decreased from 3.72±0.61 mm, 6.50±1.10 mm, 151.04±3.15 mm to 1.79±0.11 mm, 3.08±0.21 mm and 126.87±2.14 mm (p=0.007; p=0.015; p=0.001, respectively). Following inversion of the electrodes, Δx, Δy and TTW were 2.26±0.23 mm, 3.25±0.32 mm and 144.02±1.87 mm (respectively p=0.078, p=0.806 and p=0.001 as compared to anode right condition).

Conclusion: our study unravelled an overcompensation process adopted by control subjects during GVS. TTW represents a sensitive parameter to evaluate effects of electrodes inversion.

P2277
AUTONOMIC DYSFUNCTION IN DEMYELINATING POLYNEUROPATHY
D.M. Merkulova1,2, Y.A. Merkulov1,2, E.M. Rokotyanskaya1,2
1B.M. Gekht Peripheral Nervous System Diseases Diagnostic and Treatment Center, JSC, Institute of General Pathology and Pathophysiology, Russian Academy of Medical Science, Moscow, Russia

Aim: To measure the degree of autonomic dysfunction in patients with demyelinating polyneuropathy (DPNP).

Methods: Conventional electromyographic (EMG) techniques with the analysis of spontaneous activity of muscle fibres, motor unit potentials (MUP) parameters, motor nerve conduction velocity (NCV) and heart rate variations (HRV) studies of 38 DPNP patients and 23 control healthy persons. HRV were measured from the electrocardiogram (ECG) recorded at rest and the Valsalva Ratio (VR) and were expressed as the mean and the standard deviation of R-R values (MR-R and SDR-R, respectively). We also measured the coefficient of R-R variations (KR-R), where KR-R=SDR-R/100/MR-R.

Results: NCV were markedly depressed in all of the cases (100%). The needle EMG showed low spontaneous activity (32 patients – 84.2% of the cases) and late MUP changes (71.1%). The autonomic vascular disorders included tachycardia (71.1%) and orthostatic collapses (36.8%). The disturbances of perspiration led to the “dry syndrome” in most of the cases (68.4%), but 5 patients (13.2%) suffered from extremely high sweatiness. Normal KR-R values were 5.94±1.04%. SDR-R=47.5±14.7 ms, VR=1.67±0.28. The reduction of the obtained data in the DPNP patients was statistically significant (p<0.01). KR-R=3.83±1.45%, SDR-R=34.34±18.0 ms, VR=1.5±0.4. There was a correlation between the degree of the clinical picture of dysautonomia and the reduction of the autonomic parameters.

Conclusion: Autonomic dysfunction is significant in DPNP patients, is manifested mostly by tachycardia and the disturbances of perspiration and can be measured by HRV, VR and KR-R to ensure the proper treatment and monitoring of the disease.

P2278
THE EFFECT OF THERAPY WITH BOTULINUM TOXIN TYPE A ON CORTICAL SOMATOSENSORY EVOKED POTENTIALS IN PATIENTS WITH UPPER LIMB SPASTICITY
R. Opavsky, P. Otruba, P. Hlustik, R. Herzig, P. Kanovsky
Department of Neurology, Palacky University, University Hospital, Olomouc, Czech Republic
Background and aims: The exact mechanism of action of botulinum toxin type A (BTX-A) in spasticity has not been elucidated so far. Besides local effect, latest data suggest reorganization of the central nervous system mediated through afferent pathways. Parameters of cortical components of SEPs were measured in order to assess the central effects of BTX-A.

Methods: Median nerve SEPs were recorded in patients suffering from upper extremity spasticity following a supratentorial ischemic stroke. Three examinations were performed: prior to BTX-An injection (E1), 4 weeks (E2) and 12 weeks (E3) following the injection into the most affected forearm muscles. Spasticity of the affected limbs was measured with the Modified Ashworth Scale (MAS).

Results: A total of 17 patients with mean age 60.8±17.4 years were studied. In patients with left-sided spasticity significant (p<0.05) relative prolongation of latencies on the affected side, if compared to the unaffected one, was found for postcentral component P17 in E0, E1 and precentral components P22/N30 in E2. There was a trend for P17 and P 22/N30 latencies recorded from the unaffected arm to prolong from the normal values in E1 to E2 with subsequent return to normal values in E3, whereas a gradual increase of the delay in these latencies from E1 value over E2 to E3, when detected on the affected arm.

Conclusions: The results may reflect different roles of the right and left brain hemisphere in processing of afferent input, as well as a distinct cortical modulation in each hemisphere following BTX-A treatment.

P2279
P300 POTENTIAL IN SUBJECTS WITH LIVER DAMAGE OF ALCOHOL-INDUCED ETIOLOGY
M. Przybyła, W. Chudzik, A. Klimek, H. Chmielewski, B. Kaczorowska
Department of Neurology and Epileptology, Medical University in Lodz, Poland

Introduction: The consequence of drinking excessive amounts of alcohol is the damage to many organs, particularly to the liver. In liver following its fatty degeneration, comes hepatitis, fibrosis and finally cirrhosis.

Aim: The aim of the study was the analysis of P300 potential in subjects chronically abusing alcohol with alcohol-related toxic liver damage and the assessment of the usefulness of this potential in the diagnostics of hepatic encephalopathy.

Material: Group I – consisted of 30 men meeting the criteria of alcohol dependency syndrome, with diagnosed alcohol-related toxic liver damage and the assessment of the usefulness of this potential in the diagnostics of hepatic encephalopathy.

Methods: The following was carried out in all the cases examined: examination of auditory endogenic P300 potential.

Results: Mean P300 latency in group 1 was 378.1±23.1 ms; in group 2 – 317.6±17.4 ms. Mean P300 amplitude was: in group 1 – 23.1±1.90. Resting motor thresholds were 25% and 27% of stimulator output for FDI and ABP. The representational area of FDI and ABP was 5.01 cm² and 4.26 cm² respectively. This first TMS mapping in the awake monkey demonstrates that TMS is practicable, reliable and well tolerated in a properly trained monkey. The TMS-assessed primate motor representation is comparable to that of humans, being also in accordance with the current neuroanatomical data. Particularly because of its remarkably low TMS thresholds in combination with the high focality of the commercial TMS coil, the rhesus monkey represents a promising model for the investigation of long-lasting TMS assessable neuroplastic changes.

P2280
CHOLINERGIC CRISIS IN ORGANOPHOSPHATE INTOXICATION: CLINICAL AND ELECTROPHYSIOLOGICAL ASPECTS
M.A. Rafaj, F.Z. Boulaajaj1, B. Charra1, A. Benslama1, M. Bouriouzgui2, B. El Moutawakkil3, S. Motaouakkil2, I. Slassi1
1Service de Neurologie, Explorations Fonctionnelles CHU Ibn Rochd, Quartier des Hôpitaux, 2Service de Réanimation Médicale, CHU Ibn Rochd, 3Service de Neurologie, Explorations Fonctionnelles, Service de Réanimation Médicale, CHU Ibn Rochd, Quartier des Hôpitaux, Casablanca, Morocco

Introduction: The acute organophosphates intoxication (OP), accidental or voluntary, are responsible for a high mortality. They involve extensive muscular paralysis by acetyl cholinesterase activity inhibition on neuromuscular junction level.

Aim: to underline the rarity and the characteristic electrophysiological aspect during cholinergic crisis.

Observation: A 28-year-old young woman, hospitalized in medical intensive care unit for Malthion acute intoxication (OP) with signs of glandular hypersecretion, complicated tetraparesis and respiratory distress. The cholinesterase activity was at 17%. The electromyography showed multiple motor action potential (responses) to the same stimulation, characteristic of the cholinergic crisis step. Other electrophysiological parameters, in particular repetitive stimulations at low frequencies, were normal. The evolution was favourable after symptomatic treatment and respiratory assistance.

Discussions and conclusions: The organophosphates intoxications evolve in three phases: acute cholinergic crisis, intermediate syndrome and delayed neuropathy. If the electrophysiological aspects of delayed neuropathy are best characterized, those of crisis and intermediate syndrome remain very little studied. The persistence of the acetylcholine in synaptic slit would explain the multiple motor responses to single stimulation during the crisis.

P2281
GIANT F-WAVES AS A SIGN OF IMPAIRED CENTRAL MOTOR PATHWAYS IN PATIENTS WITH MYELOPATHY
A.A. Rogozhin, F.I. Devlikamova
Department of Neurology and Spine Disorders, Kazan State Medical Academy, Republican Clinical Hospital of Rehabilitation, Kazan, Russia

F-wave amplitude is rarely analyzed, while it could add valuable information on excitability of motor neurons in different disease states. We made a retrospective analysis of occurrence of giant F-waves in non-damaged segments in patients with suspected cervical myelopathy. In each subject F-waves were recorded for abductor pollicis brevis (APB) and adductor digiti minimi (ADM) using surface electrodes. F-waves were classified as giant if their amplitude was more than 10% of CMAP. Central motor conduction time (CMCT) for ADM was calculated and standard needle EMG of deltoideus, biceps brachi, extensor digitorum communis and adductor pollicis brevis muscles were done to reveal motoneuron damage. Among 273 patients with suspected cervical myelopathy 19 had abnormal CMCT to ADM from one side and no EMG changes in muscles from C5 to C8 segments. In 10 patients from that group we recorded giant F-waves. In 7 patients giant F-waves were recorded from the side opposite to increased CMCT. In 3 patients giant F-waves were recorded from both sides. Giant F-waves were recorded from APB in 4 patients (3 – from one side; 1 – from both sides); from ADM in 6 patients (4 – from one side;
MANDIBLE FRACTURE (n=2). THERMAL DETECTION AND PAIN THRESHOLDS WITH SENSORY DISTURBANCES AFTER UNILATERAL ORBITAL FLOOR (n=12) OR

SIXTY HEALTHY SUBJECTS (30 M, 30 F; 19–62 YEARS) AND 14 PATIENTS (9 M, 5 F; 18–74 YEARS) PARTICIPATED IN THE STUDY. HEALTHY SUBJECTS

BACKGROUND: PRE-ECLAMPSIA IN PREGNANT WOMEN CAUSES THE FUNCTIONAL STATE OF BRAIN DISORDERS.

AIM: TO INVESTIGATE THE BIOELECTRICAL BRAIN ACTIVITY AND AUDITORY PATHWAY IN PREGNANT WOMEN WITH PRE-ECLAMPSIA.

MATERIALS AND METHODS: WE CONDUCTED A CLINICAL, NEUROPHYSIOLOGICAL (BAEP, EEG) INVESTIGATION OF 86 PREGNANT WOMEN, AMONG THEM: WITH PRE- ECLAMPSIA (n=27, MEAN AGE 28.1±1.5), WITH PRE- ECLAMPSIA AND ACCOMPANYING NEUROLOGICAL PATHOLOGY (NP) (n=26, MEAN AGE 26.7±0.7), WITH NP WITHOUT PRE- ECLAMPSIA (n=23, MEAN AGE 25.9±1.8), AND WITH PHYSIOLOGICAL PREGNANCY (n=10, MEAN AGE 24.6±1.4).

RESULTS: IN PREGNANT WOMEN WITH PRE- ECLAMPSIA THE BAEP I-V, I-III INTER-PEAK LATENCY WAS PROLONGED IN 5 (18.5%) PATIENTS, AND THE I-V, III-V IN 3 (11.1%); WITH PRE- ECLAMPSIA AND NP IN 7 (26.9%) AND IN 3 (11.5%) RESPECTIVELY. THE NP WITHOUT PRE- ECLAMPSIA PATIENTS REVEALED THE DEVIATIONS CORRESPONDING TO THEIR NEUROLOGIC PATHOLOGY. WOMEN WITH PHYSIOLOGICAL PREGNANCY REVEALED NO CHANGES IN THE BAEP PARAMETERS. COMPARED TO PHYSIOLOGICAL PREGNANCY, IN PREGNANT WOMEN WITH PRE- ECLAMPSIA, EEG FINDINGS INDICATED DISORGANIZATION, BILATERAL NON-SPECIFIC PAROXYSMAL ACTIVITY, AND PAROXYSMAL ACTIVITY IN THE FORM OF SHARP WAVES AND SHARP- SLOW WAVE COMPLEXES. PRE- ECLAMPSIA IN COMBINATION WITH ACCOMPANYING NP SHOWED AN INCREASE OF PATHOLOGICAL ACTIVITY IN THE EEG READINGS.

CONCLUSION: BAEP AND EEG CAN BE USEFUL IN DETECTING SUBCLINICAL AUDITORY PATHWAY AND BIOELECTRICAL BRAIN ACTIVITY DYSFUNCTION IN PREGNANT WOMEN WITH PRE-ECLAMPSIA.

P2283

ASSESSMENT OF TRIGEMINAL NERVE DISORDERS BY QUANTITATIVE SENSORY TESTING

S. Said Yekta1, S. Jaenicke2, R. Smeets2, J. Ellrich1
1Department of Neurosurgery, Experimental Neurosurgery Section, 2Department of Oral, Maxillofacial and Plastic Surgery, RWTH Aachen University, Aachen, Germany

SENSORY TESTING (QST) IS APPLIED TO EVALUATE SOMatosensory NERVE FIBRE FUNCTION. COMPARSED TO SPINAL SYSTEM, THERE ARE ONLY VERY FEW INVESTIGATIONS IN THE TRIGEMINAL REGION. IN THIS STUDY, NORMATIVE DATA FOR INNERRATION AREAS OF SECOND AND THIRD TRIGEMINAL BRANCHES WERE DEFINED AND THE USEFULNESS OF QST IN THE DIAGNOSIS OF NERVE LESIONS IN PATIENTS WAS APPRAISED.

SIXTY HEALTHY SUBJECTS (30 M, 30 F; 19–62 YEARS) AND 14 PATIENTS (9 M, 5 F; 18–74 YEARS) PARTICIPATED IN THE STUDY. HEALTHY SUBJECTS WERE TESTED BILATERALLY IN INNERRATION AREAS OF INFRAORBITAL AND MENTAL NERVES. PATIENTS WERE TESTED BILATERALLY IN INNERRATION AREAS WITH SENSORY DISTURBANCES AFTER UNILATERAL ORBITAL FLOOR (n=12) OR MANDIBLE FRACTURE (n=2). THERMAL DETECTION AND PAIN THRESHOLDS (PELTIER-TYPE THERMODE), MECHANICAL DETECTION_THRESHOLD (VON-FREY_FILAMENTS), MECHANICAL PAIN_THRESHOLD AND SENSITIVITY, WIND-UP_RATIO (PINPRICK STIMULI), DYNAMIC MECHANICAL ALLODYNIA, VIBRATION DETECTION_THRESHOLD (TUNING FORK) AND PRESSURE PAIN_THRESHOLD (SPRING MOUNTED PRESSURE METER) WERE DETERMINED. COMPARISON OF PATIENT’S DATA WITH ESTABLISHED NORMATIVE DATA SHOWED WARM, COLD AND MECHANICAL HYPOESTHESIA IN 8 PATIENTS. 3 PATIENTS HAD HYPOESTHESIA TO COLD AND WARM, AND 3 ONLY TO WARM. 4 PATIENTS WERE RE- INVESTIGATED AND SHOWED CLEAR IMPROVEMENT OR NORMALISATION, RESPECTIVELY, OF CORRESPONDING PARAMETERS. QST CAN BE APPLIED FOR NON-INVASIVE ASSESSMENT OF SENSORY NERVE FUNCTION (Aβ-, Aδ- AND C-FIBRE) IN THE TRIGEMINAL REGION AND ALLOWS MONITORING OF SENSORY FUNCTIONS IN TIME COURSE. QST CAN BE REGARDED AS USEFUL IN THE DIAGNOSIS OF TRIGEMINAL NERVE DISORDERS IN PATIENTS.

P2284

FREQUENCY OF PHOTSENSITIVE RESPONSES IN A COHORT OF ADULT EPILEPTIC PATIENTS

M. Mobin1, A. Saeed3, M. hashmi3, A. Bano1, A. Malik1, F.S. Khan1, K.A. Siddiqui1
1Department of Neurology, 2Department of Clinical Neurophysiology, Liaquat National Hospital, Karachi, Pakistan

BACKGROUND AND AIMS: WE WANTED TO KNOW ANY CAUSAL RELATIONSHIP BETWEEN PHOTIC DRIVING AND PHOTOCONVULSIVE RESPONSE AND TO DETECT FREQUENCIES OF THESE RESPONSES ON INTERMITTENT PHOTIC STIMULATION IN ADULT PATIENTS WITH DIFFERENT FORMS OF EPILEPSY.

METHODS: WE RETROSPECTIVELY COLLECTED DATA FROM 2003–2006, OF ALL PATIENTS REFERRED TO EEG DEPARTMENT, AGED 15 AND ABOVE. WE THEN SEPARATED THOSE EEG’S WHICH HAD ‘ANY RESPONSE’ TO PHOTIC STIMULATION. NORMAL RESPONSES INCLUDED PHOTIC DRIVING RESPONSE, VISUAL EVOKED RESPONSE AND PHOTOMYOCLOTONIC RESPONSE. ABNORMAL RESPONSES INCLUDED PHOTOCONVULSIVE RESPONSE. WE ALSO LOOKED AT REASON FOR EEG REFERRAL AND UNDERLYING EPILEPSY SYNDROME.

RESULTS: THERE WERE 5950 EEG’S PERFORMED OVER THESE FOUR YEARS, IN PATIENTS AGED 15 AND ABOVE. WE NOTED 1.2% (n=73) PATIENTS HAD ‘ANY RESPONSE’ TO PHOTIC STIMULATION. OUT OF WHICH 67.1% (n=49) PATIENTS HAD NORMAL RESPONSE AND 32.8% (n=24) HAD ABNORMAL RESPONSE. PHOTIC DRIVING WAS THE ONLY NORMAL RESPONSE FOUND IN 100% (n=49) PATIENTS. ALL PATIENTS WHO HAD PHOTOCONVULSIVE RESPONSE, NONE OF THEM HAD NORMAL RESPONSE. OF THESE 58.3% (n=14) HAD PRIMARY GENERALIZED EPILEPSY, 41.1% (n=1) HAD SECONDARY GENERALIZED EPILEPSY, 37.5% (n=9) HAD PARTIAL EPILEPSY. REASON FOR EEG REFERRAL IN THIS COHORT WAS GENERALISED TONIC CLONIC SEIZURE IN 43.8% (n=32), MYOCLOTONIC SEIZURE IN 6.8% (n=5), ABSENCE SEIZURE IN 5.5% (n=4) AND UNIDENTIFIED SEIZURE IN 43.8% (n=32) OF PATIENTS.

CONCLUSION: WE FOUND THAT THERE IS NO RELATIONSHIP BETWEEN PHOTICDRIVING RESPONSE TO PHOTOCONVULSIVE RESPONSE IN ADULT EPILEPTIC PATIENTS. ABOUT 0.8% OF PATIENTS HAD PHOTICDRIVING RESPONSE AND 0.4% HAD PHOTOCONVULSIVE RESPONSE TO INTERMITTENT PHOTIC STIMULATION. FREQUENCY OF PHOTOCONVULSIVE RESPONSE WAS HIGHER IN PATIENTS WITH PRIMARY GENERALIZED EPILEPSY FOLLOWED BY PARTIAL EPILEPSY.

P2285

K(ATP) CHANNEL-DEPENDENT GABA OUTFLOW IS ASSOCIATED WITH LEPTIN RECEPTOR EXPRESSION IN THE RATS’ CAUDATE NUCLEUS

M. Steinkamp, H. Fuellgraf, M. Kolbe, A. Moser
Department of Neurology, University of Lübeck, Germany

K(ATP) CHANNELS COUPLE THE BIOENERGETIC METABOLISM TO MEMBRANE EXCITABILITY. IN OUR PREVIOUS STUDIES WE COULD DEMONSTRATE...
that GABA-mediated inhibition of dopamine outflow was regulated by high and low affinity K(ATP) channels in the rat caudate nucleus. Homozygous leptin receptor (LR)-deficient Fa/Fa rats are obese and sometimes diabetic (ZDF=Zucker diabetic fatty rat). Since LR activity is linked to K(ATP) channel functioning, we used slices of the caudate nucleus from ZDF Fa/Fa, Fa/+, and control rats to study the effect of K(ATP) channels on GABA outflow. Slices were incubated in superfusion chambers and GABA outflow was measured by means of HPLC with ECD. After preincubation, extracellular glucose concentrations were reduced from 10 to 7 mM. Under these conditions GABA outflow decreased from 6.9±2.0 nM to 3.2±1.6 nM in striatal slices of control rats. In contrast, in Fa/Fa as well as in Fa/+ rats GABA outflow remained nearly unchanged when extracellular glucose levels were lowered. The K(ATP) channel-blocker glibenclamide (Glb, 10 μM) prevented GABA outflow reduction in control rats at glucose concentrations of 7 mM implying that K(ATP) channels were involved. Under Glb conditions no change of GABA outflow was observed in heterozygous and in homozygous ZDF Fa/Fa animals. These results led us to suggest that K(ATP) channel-dependent GABA outflow is associated with leptin receptor expression in the rat caudate nucleus. Although heterozygous Fa/+ rats possess one healthy LR allele no difference could be observed between heterozygous and homozygous animals. This is unexpected and should be clarified in further experiments.

P2286
COULD SECOND LUMBRICAL INTEROSSEI TESTING BE STRATEGIC TO REDUCE THE NUMBER OF TESTS FOR DIAGNOSING CARPAL TUNNEL SYNDROME?

T. Aravinda Kannan1, E. Li2, E. Wilder-Smith3
1Department of Neurology, National University Singapore, 2Department of Neurology, National University Hospital, Singapore

Background: The Second Lumbrical Interosseae Latency difference test (2LINT) is frequently used to support a diagnosis of carpal tunnel syndrome (CTS). Recently the pre-motor potential (2LPMP) observed with 2LINT was identified as a median sensory potential. 2LINT recording therefore not only compares conduction across equidistant median and ulnar motor segments, but also registers median sensory conduction.

Aim: We tested whether motor and sensory data solely obtained with 2LINT may be strategic in reducing the numbers of tests necessary for CTS testing.

Methods: A prospective study at the National University Hospital, Singapore. Patient inclusion criteria were a clinical diagnosis of CTS which was established in the presence of at least two of the four primary symptoms of CTS. Exclusion criteria: Patients with weakness or wasting of ulnar-innervated muscles, primary neck symptoms or proximal nerve pathology, diabetes, uremia and hypothyroidism. Nerve conduction performed: median digit 3 sensory conduction (3MS), abductor pollicis brevis latency (APB), 2LPMP peak latency, 2LINT and ulnar 2nd interossei motor conduction (UI) – 2LPMP latency difference.

Results: A total of 102 hands were tested (52 controls, 50 CTS). Sensitivity and specificity for 3MS and APB was 81/94% and 71/96%. Sensitivity of 2LINT derived parameters was: 2LINT: 75%; 2LPMP: 77%; UI-2LPMP: 79%; specificity identical (94%). Overall highest sensitivity (87%) was achieved by combining 2LINT parameters.

Conclusion: The 2LINT technique by simultaneously co-registering motor and sensory median and ulnar motor nerve function may be strategic to reduce the number of tests necessary to support a diagnosis of CTS.

P2287
DEMOGRAPHIC CHARACTERISTICS OF MENIERE’S DISEASE IN ARDABIL

A. Abedi1, B. Sotode1, M. Jafari2
1Physiology Department, 2Neurology Department, Faculty of Medicine, ‘Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

P2288
MAGNESIUM DEFICIENCY AND AUTONOMIC SYSTEM

E. S. Akarachkova1, S. B. Shvarkov2
1Department of Autonomic Disorders, Moscow Medical Academy RAMS, Moscow, Russia

P2289
CORTICAL EXCITABILITY CHANGES AFTER REPETITIVE THUMB TRAINING, A TMS STUDY IN STROKE PATIENTS AND HEALTHY SUBJEC

T. I. Blicher1, J. F. Nielsen2
1Hammel Neurocenter, Hammel, 2Aarhus University Hospital, Aarhus, Denmark

P2290
THE USE OF ACCELEROMETRY IN BELARUS

V. V. Ponomarev, A. V. Boika
2nd Neurological Department, 5 City Clinic, Minsk, Belarus

P2291
VERTEBROBASILAR DOLichoektasia with Autonomic Symptoms and Therapeutic Considerations – A Case Report

R. L. Gheorghe Dane1, C. A. Sirb1, O. Sirbu1, L. Ionescu1, R. S. Nitu1, E. Chirca2
1Department of Neurology, Central Clinical Military Emergency Hospital, Bucharest, 2Department of Cardiology, Emergency District Hospital, Ploiesti, Romania

P2292
Abstract cancelled

P2293
THE CORRECTION OF PSYCHO-NEUROLOGICAL DISORDERS OF PATIENTS WITH PAROXYSMAL VEGETATIVE DISTURBANCES

S. V. Seleznova1, O. O. Zabara2
1Neurological Department, Donetsk State Medical University, 2Regional Rheumatological Center, Donetsk Regional Clinical Territorial Medical Union, Donetsk, Ukraine

P2294
EEG DETECTION OF SEIZURE ACTIVITY

I. Shekhovtsev
Psychology Department, SU-HSE, Moscow, Russia

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
P2295
VARIous diseases and environment as risk factors in the formation of autonomic disturbances
F. F. Yakhina
Kazan Medical Academy, Kazan, Tatarstan, Russia

Child and developmental neurology; Neurogenetics

P2296
TWO NOVEL CONNEXIN32 MUTATIONS CAUSE EARLY ONSET X-LINKED CHARCOT-MARIE-TOOTH DISEASE
G. J. Braathen1,4, J. C. Sand2, G. Bukholm2,3, M. B. Russell1,4
1Faculty Division, Akershus University Hospital, University of Oslo, Nordbyhagen, 2Institute for Clinical Epidemiology and Molecular Biology (Epi-Gen), Akershus University Hospital, Loerenskog, 3Department of Laboratory Medicine, Genetic Section, Telemark Hospital, Skien, 4Department of Neurology, 5Department of Research and Development, Akershus University Hospital, Loerenskog, Oslo, Norway

Background: X-linked Charcot-Marie Tooth (CMT) is caused by mutations in the connexin32 gene that encodes a polypeptide which is arranged in hexamer array and form gap junctions.

Methods: We describe two novel mutations in the connexin32 gene in two Norwegian families.

Results: Family 1 had a 225delG which causes a frameshift and premature stop codon at position 247. This probably results in a polypeptide which is not arranged in a hexamer array due to the change in protein structure. Affected persons had an early onset age usually in the first decade and several abortions were observed in the family. Family 2 had a 536 G→A transition which causes a change in the highly conserved cysteine residue to tyrosine at amino acid position 179. Thus, one of three disulfide bridges in the polypeptide is disrupted. This possibly leads to a severe structural change in the protein conflicting with formation of normal gap junctions. One man had pathological visual evoked potentials (VEP). The mean age at onset was in the first decade. Affected had symmetrical clinical findings, while the neurophysiology revealed minor asymmetrical findings in nerve conduction velocity in 6 of 10 affected.

Conclusions: The two novel mutations in the connexin32 gene are more severe than the majority of previously described mutations possibly due to the severe structural change of the gap junction they encode.

P2297
RECESSIVE SCAPULOPERONEAL SPINAL MUSCULAR ATROPHY
M. Ciumas, V. Sacara
Scientific Department, National Centre of Reproductive Health and Medical Genetic, Chisinau, Moldova

Introduction: Scapuloperoneal (SP) syndromes are heterogeneous neuromuscular disorders caused by defect of anterior horn cell. These are characterized by weakness in the distribution of shoulder girdle and peroneal muscles. Locus of dominant form of SP syndrome (scapuloperoneal muscular dystrophy) has recently been assigned to chromosome 12q24.1-q24.31. Recessive and X-linked forms have not been assigned yet. We investigated 4 unrelated patients with sporadic SPSMA (probably recessive form) for deletion in SMN locus which maps to chromosome 5q13.

Materials and methods: 4 unrelated patients with risk of SPSMA passed clinic-neurological, electromyography investigations and molecular study. DNA preparations were made from peripheral blood samples by routine methods and used for PCR. The EcoRV enzyme is necessary of digestion the PCR product of exon 7 (150bp) and BseNI enzyme is necessary of 8 exon (183bp) for distinguish SMN1 gene and its copy gene.

Results: Two patients were shown to have a homozygous deletion in exon 7 of the SMN1 gene, although exon 8 was present. Another patient had deletion of both exons 7 and 8 of the SMN1. The 4th patient revealed a decreased ratio of SMN1 and SMN2-specific bands, which is most probably explained by a deletion of SNM1 in a chromosome.

Conclusions: Taking into account a strong association between SMN1 gene mutation and both SMA and SPSMA, and the phenotypic similarities between the two disorders, it could be concluded that SMA locus is also responsible for SPSMA phenotype in families with autosomal recessive inheritance.

P2298
A NOVEL HETEROPLASMIC tRNAser (CUN) mtDNA POINT MUTATION FIRST ASSOCIATED WITH PROGRESSIVE EXTERNAL OPHTHALMOPLAGIA
E. Cardaioli1,2, P. Da Pozzo1, G. N. Gallus1, A. Malandrini1,2, S. Gambelli1, C. Gaudiano1, G. Berti1, G. Serni1, M. T. Dotti1, A. Federico1
1Department of Neurological and Behavioural Sciences, University of Siena, Italy, 2Associazione Anni Verdi, Rome, Italy

Background: Progressive external ophthalmoplegia (PEO), one of the most common mitochondrial clinical phenotypes, in more than 60% of cases is associated with large-scale rearrangements of mitochondrial DNA (mtDNA), while point mutations of tRNA genes represent the second most common genetic cause (Mitomap: http://www.mitomap.org).

Aim: to perform a molecular diagnosis in a patient with sporadic chronic external ophthalmoplegia (CPEO) and 5% of COX-negative fibres at muscle biopsy, which had no detectable large mtDNA deletions.

Methods: Total DNA was extracted from various tissues of the proband and his mother. All the mitochondrial tRNA genes were amplified by polymerase chain reaction and directly sequenced.

Results: Direct sequencing failed to detect mutations previously reported and showed a heteroplasmatic mutation at nucleotide 7506 in the tRNAser (CUN) gene, in the dihydrouridine stem, which is highly conserved between species during evolution. RFLP analysis confirmed that approximately 30% of muscle and 20% of urinary epithelium mtDNA harboured the mutation, while it was absent in lymphocyte, hair bulbs and buccal epithelium mtDNA of the proband as well as in lymphocyte, buccal epithelium and muscle DNA of his mother and 100 patients affected by various encephalomyopathies.

Conclusion: To date, behind large and single nucleotide deletions, several point mutations on mitochondrial tRNA genes have been reported in CPEO patients, but between them no one was reported in the gene coding for tRNAser (CUN), so our mutation is the first associated with this phenotype.
P2299

A NOVEL MNGIE MUTATION
University Department of Clinical Neurosciences, Hampstead Campus, Royal Free and University College Medical School, University College London, London, UK

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is an autosomal recessive disease caused by mutations in the gene for thymidine phosphorylase (TP). The clinical features comprise:

1. Peripheral neuropathy,
2. Symptoms of gastrointestinal dysmotility,
3. Asymptomatic cerebral white matter lesions, and
4. Mitochondrial myopathy.

We report a 22-year-old woman who presented with a 15-year history of recurrent episodes of diarrhoea, vomiting and abdominal pain. She had bilateral ptosis, partial external ophthalmoplegia and sensorineural hearing impairment. There was generalised muscle wasting and weakness in the limbs. Tendon reflexes were absent. Thymidine and deoxyuridine were detected in her plasma, and TP enzyme activity was absent in leucocytes and platelets, confirming a diagnosis of MNGIE. Sequencing the patient’s TP gene revealed two heterozygous mutations: one intronic G to C transversion bordering exon 3 (g.675G>C) and one intronic G to A transition bordering exon 9 (g.4009G>A). Both mutations are predicted to affect messenger RNA splicing, rendering their alleles non-functional.

The g.4009G>A mutation has not been described previously. A non-functioning TP gene will perturb mitochondrial nucleotide pools, with resulting secondary mitochondrial (mt) DNA abnormalities. The patient’s muscle biopsy showed an excess of cytochrome oxidase negative fibres, which also stained negative with an antibody to the mtDNA-encoded subunit I of cytochrome oxidase. Multiple mtDNA deletions were demonstrated in the muscle sample.

P2300

THE SIGNIFICANCE OF APOLIPOPROTEIN E GENE AND ANGIOTENSIN-CONVERTING ENZYME GENE IN THE DEVELOPMENT OF INTRACRANIAL ANEURYSMS IN RUSSIAN POPULATION
E.R. Lebedeva1, V.P. Sakovich1, R.I. Khusainova2, I.A. Kutuev2, R.R. Valleve3, N.N. Khushnutdinova3, E.K. Khushnutdinova3
Department of Neurology and Neurosurgery, The Urals State Medical Academy, Ekaterinburg, Institute of Biochemistry and Genetics, Russian Academy of Sciences, Ufa, Russia

Background: The aim of our study was to determine the role of apolipoprotein E gene (APOE) and angiotensin-converting enzyme gene (ACE) in the development of intracranial aneurysms (IA) and associations of these genes with significant risk factors for IA in Russian population.

Methods: The study population consisted of 166 patients with IA (83 men and 83 women, mean age 43.5 years) and 192 control subjects – healthy blood donors without IA (107 men and 85 women, mean age 43.8 years). We collected pedigrees in both groups of these patients and obtained information about risk factors for IA using clinical interview, results of examinations and all available medical documentation. For detection of APOE and ACE genes polymorphism, the standard PCR method was performed using genomic DNA isolated from peripheral blood leukocytes.

Results: We found increased risk for development of IA in e2 carriers and e2/e3 subjects who had the following risk factors: family history of intracranial haemorrhages (χ²=5.34, p=0.025 – for e2 and χ²=5.82, p=0.025 for e2/e3) and family history of IA (χ²=7.37, p=0.01 and χ²=9.88, p=0.005 respectively). Besides we revealed increased risk of development of IA in hypertensive women with family history of arterial hypertension who had e2/e3 genotype of APOE gene (χ²=4.58, p=0.032) and in hypertensive men with DD genotype of ACE gene (χ²=3.57, p=0.05).

Conclusion: Our results suggest that APOE may represent an important candidate gene for development of IA in Russian population. The role of ACE gene is less significant.

P2301

Abstract cancelled

P2302

CLINICAL AND GENETIC STUDY OF 11 ITALIAN PATIENTS WITH PARAPLEGIN GENE MUTATIONS (SPG7)
C. Mariotti, D. DiBella, M. Plumari, V. Fracasso, R. Fancellu, S. DiDonato, S. Baratta, C. Gellera, F. Taroni
Fondazione IRCCS, Istituto Neurologico C.Besta, Milan, Italy

Mutations in the SPG7 gene are responsible for autosomal recessive spastic paraplegias (HSP). This gene encodes paraplegin, a major component of the mitochondrial mAAA metalloprotease. We sequenced the paraplegin gene in 74 unrelated index cases, including 53 sporadic cases and 21 cases compatible with autosomal recessive inheritance. Paraplegin expression was investigated using polyclonal antibodies raised in our laboratory. Pathogenic mutations (3 frameshift, 4 nonsense, 1 in-frame exon deletion, 1 splicing, and 5 missense including the Ala510Val) were found in 14 sporadic patients and in 1 familial case. 10 sporadic patients (10/53, 18.9%) and 1 patient in the familial group (1/21, 4.8%) had mutations on both alleles. Western blot analysis of lymphocytes demonstrated the absence of paraplegin protein in the 4 patients carrying null alleles, and a great reduction of protein levels in a patient homozygous for the Ala510Val mutation. The study of the clinical features indicate that paraplegin mutations are associated with a late onset progressive neurodegenerative disorder (mean age at onset 51 ± 10 years), characterized by either pure spastic paraparesis, or by a complex form in which cerebellar ataxia is often associated. MRI studies confirmed the main involvement of the cerebellar structures. Skeletal muscle investigations did not reveal morphological or biochemical abnormalities. In our study, SPG7 mutations account for 14.9% of HSP patients. Analysis of protein levels indicates that the Ala510Val substitution is a disease-causing mutation. Spastic paraplegia and cerebellar signs characterize the phenotype of SPG7 patients.

[Partly supported by Telethon GUP04009 and Fondazione Mariani R0544 to FT]

P2303

SPINOCEREBELLAR ATAXIA TYPE 17: CLINICAL AND GENETIC STUDIES IN A LARGE SERIES OF ITALIAN PATIENTS
C. Mariotti1, R. Fancellu1, D. Alpini1, P. Soliveri1, A. Castucci1, C. Gellera1, F. Taroni1, S. DiDonato1
1Fondazione IRCCS, Istituto Neurologico C.Besta, 1ENT-Otorhinolaryngology Service, Istituto S. Maria Nascente, Milan, Italy

SCA17 is an autosomal dominant spinocerebellar ataxia caused by a CAG/CAA expansion in the gene encoding the TATA-binding
protein (TBP). We screened for the SCA17 mutation in 110 subjects with progressive cerebellar ataxia and 94 subjects with Huntington-like phenotype. 15 subjects (11 affected and 4 pre-symptomatic individuals) from 7 unrelated Italian families were found to carry expanded alleles with $\geq 45$ CAG repeats. 2 patients were sporadic cases, 4 patients (2 families) had familial spinocerebellar ataxia, and 5 patients (3 families) had a family history for psychiatric and movement disorders. 8 subjects carried 45 CAG repeats, one patient carried 46 repeats, while 5 subjects had expansions larger than 50 repeats. All mutated subjects in each family carried the same size of CAG expansion. Age at onset ranged from 19 to 55 years. Cerebellar signs and symptoms were present in all cases; 80% of the patients had mild to severe cognitive deficits; 66% of patients showed choreic movements; pyramidal signs, bradikynesia and dystonia were observed in approx 50% of the cases. MRI demonstrated cortical and cerebellar atrophy. No deficits in the peripheral nervous system were identified. Oculographic examinations showed a distinct pattern of oculomotor findings, characterized by impairment of smooth pursuit, defects in saccade accuracy, but normal saccade velocity, and absence of nystagmus. This study presents one of the largest series of SCA17 patients in Europe. Our data confirm the large variability in SCA17 phenotypic presentation, and indicate that a peculiar combination of neuroradiological, electrophysiological and oculomotor findings is recognizable in SCA17.

P2304

COMPARTMENTAL EXPRESSION OF FOXP2, A GENE INVOLVED IN SPEECH AND LANGUAGE, IN THE DEVELOPING PRIMATE STRIATUM

K. Takahashi1,2, F-C. Liu3, K. Hirokawa3, H. Takahashi1
1Developmental Neurobiology Group, Mitsubishi Kagaku Institute of Life Sciences, 2Department of Pathology, Tokyo Medical and Dental University, Tokyo, Japan, 3Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan-R.O.C.

Background: FOXP2 has recently been identified as the first gene that was linked to an inherited form of language and speech disorder. The neuropathology for language deficit in the patients with FOXP2 mutation has not been reported and even the expression of FOXP2 in the human brain has not been completely investigated.

Methods: Because of the restricted availability of the human materials and the ethical limitation, we performed a developmental study of the expression pattern of FOXP2 mRNA in the developing and adult non-human primate brain, use of which enables us to examine the expression in the immature brain at the perinatal period in detail.

Results: We found that FOXP2 mRNA was expressed in several structures of the central nervous system including the cerebral cortex, striatum and thalamus in the immature brain, but not in the adult. Of interest, FOXP2 was expressed in the striosomal compartment of the caudate nucleus and the putamen in the prenatal brain and the expression was only detected in the caudate nucleus at the early postnatal stages.

Conclusion: The preferential expression of FOXP2 in the caudate nucleus in which the striosomes are more prominent may account for the fact that the caudate nucleus is one of the primary affected brain regions in the patients with FOXP2 mutation revealed by morphometric and functional anatomical studies using MRI and PET. Our study also supports the viewpoints that the caudate nucleus plays an important role in the language processing as suggested by recent neuropsychological and imaging studies.

P2305

DEVELOPMENT OF CHILD NEUROLOGY IN SERBIA AND FUTURE PERSPECTIVES

N. Todorovic, T. Miletic-Drakulic
Department of Neurology, Clinical Centre Kragujevac, Kragujevac, Serbia

Development of child neurology in Serbia is closely linked to the Clinic of Neurology and Psychiatry for Children and Adolescents in Belgrade. This institution was established from the neuropsychiatric clinic in Belgrade in 1950. In 1993, by the decision of health regulators, education in child neurology and child psychiatry was postulated as separate specialities. Till then a specialty like this did not exist, but only education as subspecialty in this field of interest. A separate specialty in child neurology in Serbia lasts 4 years. The specialty includes practical training for 39 months as well as theoretical teaching for 9 months at Belgrade University. Practical training includes training at most in child neurology at Clinic for Neurology and Psychiatry for Children and Adolescents in Belgrade, which is the only referent institution for training in this field, and some in adult neurology, paediatrics, child psychiatry, neurosurgery, ophthalmology, otorhinolaryngology, and infectious diseases. From 1993 until today 15 child neurologists completed their education. Except the specialty, Clinic for Neurology and Psychiatry for Children and Adolescents in Belgrade, and Belgrade University, offer training in child neurophysiology, continuous education in epileptology, genetics etc., as well as postgraduate studies in different fields of child neurology.

In our opinion, this education will continue its development in future, in tendency to reconcile with an educative program of the European Union.

P2306

HYPOXIC STRESS RESPONSE IN DEVELOPING MOUSE BRAIN: EFFECTS OF LEVETIRACETAM (LEV) ON HIF-1-DEPENDENT VASOACTIVE FACTORS

R. Trollmann1,2, J. Schneider1, D. Wenzel1, W. Rascher1, O.O. Ogunshola2, M. Gassmann2
1Department of Paediatrics, University of Erlangen, Erlangen, Germany, 2Institute of Veterinary Physiology, Vetsuisse Faculty and Zurich Centre for Integrative Human Physiology ZIHP, University of Zurich, Switzerland

Background: As the antiepileptic drug LEV decreased cellular damage in cerebral ischemia, we aimed to prove its effects on hypoxia inducible transcription factor (HIF)-1-regulated adaptive systems in the developing brain.

Objective: To study effects of LEV on HIF-1alpha, the O2-dependent HIF-1-subunit, and HIF-1-regulated targets (VEGF, iNOS) in the developing mouse brain under global hypoxia at postnatal day 0 (P0) and 7 (P7).

Material and methods: Foetal C57BL/6 mice (P0, P7) were treated with saline or LEV (i.p.; 50 mg/kg) 1 h before exposure to normoxia (N, 21% O2) or systemic hypoxia (H, 8% O2, 6 h). HIF-1alpha protein was detected by immunohistochemistry. Gene expression was quantified by TaqMan RT PCR.

Results: (mean±SEM). Under normoxia, no significant changes of cerebral HIF-1alpha, VEGF and iNOS expression were observed in LEV-treated (P0, n=6; P7 n=7) compared to control mice (P0, n=6; P7, n=7). Hypoxia itself led to prominent accumulation of HIF-1alpha as well as significant up-regulation of VEGF at P0 (N, 0.022±0.001, n=6; H, 0.031±0.003, n=6) and P7 (N, 0.096±0.032, n=7; H, 0.873±0.069, n=7; p<0.001). Interestingly, iNOS mRNA levels significantly decreased in hypoxic
brains at P0 (N, 1,001±0.057; H, 0.733±0.048, p=0.01) and at P7 (N, 1.364±0.083; H, 0.319±0.047, p<0.001). LEV did not substantially affect HIF-1alpha protein, VEGF and INOS mRNA levels in the hypoxic cortex compared to controls. **Conclusions:** Activation of HIF-1alpha represents an early response of the developing brain to short-term hypoxia in vivo. There was no evidence of toxic effects of LEV on HIF-1alpha. LEV did not significantly alter crucial endogenous, HIF-1-regulated neuroprotective mechanisms.

P2307
**HEREDITARY SPASTIC PARAPLEGIA CAUSED BY THE NOVEL MUTATION 1047INS C IN THE SPG7 GENE**

C. Tzoulis¹, P.S. Denora², L.A. Bindoff³
¹Department of Neurology, Institute of Clinical Medicine, University of Bergen and Haukeland University Hospital, Bergen, Norway, ²Department of Molecular Medicine and Neurosciences, IRCCS Bambino Gesù Hospital, Rome, Italy

Spastic paraplegia type 7 (SPG7) is an autosomal recessive form of hereditary spastic paraparesis (HSP) caused by mutations in the nuclear gene encoding the mitochondrial protein paraplegin. Paraplegin is a subunit of an ATP-dependent AAA-protease located within the inner mitochondrial membrane and is thought to be involved in the processing and degradation of mitochondrial proteins. Paraplegin mutations cause HSP with either a pure or complex phenotype. We have identified a novel paraplegin mutation, 1047insC, in a non-consanguineous Norwegian family with a recessively inherited HSP. The mutation was absent in 250 controls. This is the first description of SPG7 in the Norwegian population. Onset was relatively late (35-45y) and the clinical phenotype was essentially pure. However, 2 patients had in addition mild ptosis. Paraclinical investigations were essentially unremarkable with the exception of muscle biopsy which interestingly revealed the presence of ragged-red and cytochrome oxidase negative fibres.

P2308
**STUDY OF SOME SERUM TRACE ELEMENTS IN CHILDREN WITH AUTISTIC DISORDER**

F.I. Kamel¹, H.H. Abdel-dayem², H.H. Elmaazhy³, A.I. Kamel³
¹Pediatrics Department, Faculty of Medicine, ²Chemical Pathology Department, Medical Research Institution, Alexandria University, Alexandria, Egypt

Autistic disorder is listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) as one of five pervasive developmental disorders (PDDs) collectively referred to as autistic spectrum disorder. The etiology of autism depends on genetic susceptibility. Thereafter, various environmental factors are suspected of precipitating the condition. The aim of this study was to assess trace elements level in the sera of children diagnosed with autistic disorders. The study was carried out on 40 children diagnosed with autistic disorder and 20 normal children (siblings of the studied cases), matched as regard age and sex. All the children that were included in the study (cases and controls) were subjected to the following:

1- full history taking and clinical examination
2- audiometric assessment
3- chromosomal study
4- diagnosis of autism was based on:
   i- the criteria listed on in (DSM-IV)
   ii- Childhood Autism Rating Scale (CARS)
5- measuring: serum level of iron, zinc, copper, cadmium and lead

We detected significant imbalance of trace elements levels in the autistic children (Low Zinc and Magnesium, high Lead and Cadmium) as compared with (siblings) control. In conclusion, this imbalance can be ameliorated by supplementing the autistic children with Zinc and Magnesium, limiting environmental exposure to heavy metals and using chelating therapy when indicated. Correcting the trace elements imbalance should theoretically improve the clinical picture of autism.

P2309
**DIAGNOSIS DIFFICULTIES IN AUTOSOMAL RECESSIVE ATAXIAS, INCLUDING SPASTIC ATAXIA OF CHARLEVOIX-SAGUENAY**

A. Andrikopoulou¹, M-J.M. Dupuis², P. Ribai³
¹Department of Neurology, Clinic Saint-Pierre, Ottignies, ²IPG Centre de Génétique Humaine, Gosselies, Belgium

**Introduction:** Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a rare syndrome characterized most by early onset spastic ataxia associated with sensorimotor neuropathy and hypermyelinated retinal fibres. It was first described in the area of Charlevoix-Saguenay in Quebec, Canada, where two founder mutations in the SACS gene were identified in homozygous or compound heterozygous state. ARSACS was also described in other European, Turkish, Japanese or Tunisian populations, but retinal abnormalities were less common. Mutations in the SACS gene in these populations were different from those found in the Canadian patients and are available only on a research basis

**Cases report:** We report the clinical history of a Belgian brother and sister who present a progressive spastic ataxia since the age of 18 years. Their family history was compatible with autosomal recessive transmission. Both patients had gait unsteadiness, brisk reflexes, with Hoffman and Babinski signs and slurred dysarthria, but no prominent myelinated retinal fibres at fundoscopy. There was no vitamin E deficiency, no hypercholesterolemia, hypoalbuminemia or elevated alpha-fetoprotein. Friedreich ataxia was ruled out by molecular analysis. Cerebral MRI showed atrophic brain stem and cerebellum. Neurophysiological studies showed signs of severe sensorimotor demyelinating neuropathy, with absent sensory action potential, increased motor distal latency and low conduction velocities. Molecular study of the SACS gene is in progress.

**Conclusion:** These cases illustrate the diagnosis difficulties in non-Friedreich, non AOA recessive ataxias. After biochemical work-up, genetic studies can contribute to the diagnosis, including spastic ataxia of Charlevoix-Saguennay without specific ophthalmologic abnormalities.

P2310
**PHENOTYPIC HETEROGENEITY IN FAMILIA CREUTZFELDT-JAKOB’S DISEASE**

C. Balla, S. Tsounis, N. Taskos, I. Milonas
Department of Neurology B’, Ahepa Hospital, Aristotle University, Thessaloniki, Greece

**Introduction:** Creutzfeldt-Jakob disease (CJD) is a rare progressive and fatal brain disorder. Characteristic symptoms are rapidly progressing dementia, hallucinations and myoclonus. Sporadic (85%), iatrogenic (5%) and familial (5–10%) forms are described.
Sporadic forms arise around 60 years of age and are associated with typical periodic complexes on electroencephalogram (EEG). Familial CJD is linked to mutations in the gene PRNP located at chromosome 20 that controls formation of the normal prion protein. They are inherited in an autosomal dominant pattern. They have earlier onset, more prolonged course and usually are lacking the typical EEG.

**Patient:** A 78-year-old Jewish woman presented with gait disturbance, memory problems, disorientation, visual hallucinations and myoclonus developed in 10 days. Her sister and her sister’s son died from CJD at the age of 40 and 51 respectively, 18 months after onset of the symptoms. Lumbar puncture revealed elevated levels of protein 14-3-3. MRI showed atrophy of frontal and temporal lobes. EEG showed typical periodic complexes of spike activity. Genetic analysis revealed the E200K mutation in the PRNP gene which accounts for >70% of familial CJD. The patient died 40 days after the onset of the disease.

**Conclusion:** Familial CJD is rare with higher incidence among Jews. Although the clinical course of familial CJD usually differs from the sporadic form, this case suggests that phenotypic variability occurs even in the same family, in terms of disease duration and EEG modifications. Differential diagnosis cannot be based on these criteria.

**P2311**

**EVIDENCE FOR DIVERSITY AND FUNCTIONAL POTENTIAL OF NEUROPROTECTIVE HUMANIN PEPTIDES**

M. Bodzioch, K. Lapicka-Bodzioch, B. Nowak, A. Dembinska-Kiec

Department of Clinical Biochemistry, Jagiellonian University, Collegium Medicum, Krakow, Poland

**Background:** Humanin is a newly identified mtDNA-encoded 24-amino acid peptide with a broad spectrum of neuroprotective and antiapoptotic properties, conferring protection against Alzheimer’s disease and stroke. Using bioinformatic tools, we have recently identified 13 putative humanin isoforms encoded within the nuclear genome.

**Aims:** To demonstrate that nuclear humanin isoforms are expressed in human tissues and show functional response to proapoptotic stimuli.

**Methods:** We performed a quantitative gene expression analysis of humanin isoforms in a standard panel of ten human tissues, including adult and fetal brain, and in human umbilical vein endothelial cells (HUVECs) exposed to a proapoptotic compound, staurosporine.

**Results:** We were able to detect expression of 10 out of 13 putative nuclearly-encoded humanin isoforms. The isoforms encoded in chromosomes 5q, 6q, 10q, 11p, 20q, and Xp showed high expression rates in the brain. In HUVECs incubated with 0.01 μM staurosporine all of the isoforms followed the same pattern of change in expression up to a four-fold initial down regulation at 6 hours, which reversed to a 2–16-fold increase above the baseline after 24 hours.

**Conclusions:** At least ten nuclearly-encoded humanin isoforms are likely functional peptides, distinct from the prototype mitochondrial humanin, but similarly able to respond to proapoptotic stimuli. Some of them are highly expressed in the brain, implying their role in neuroprotection.

Supported by grants PBZ-KBN-124/P05/2004/4 and 2 P05A 006 29 from the Polish Ministry of Science and Higher Education.

**P2312**

**TUMOR NECROSIS FACTOR-A(-308) GENE POLYMORPHISM AND TRAUMATIC BRAIN INJURY**

E. Dardiotis1, M. Dardioti1, K. Aggelakis1, A. Komnos1, A. Tasiou2, K. Paterekis2, S. Raji1, G. Xiromerisiou1, J. Gabranis4, A. Papadimitriou1, G.M. Hadjigeorgiou1

1Department of Neurology, University Hospital of Larissa.
2Department of Neurosurgery, University Hospital of Larissa, University of Thessali, 3Intensive Care Unit, 4Department of Pathology, General Hospital of Larissa, Greece

**Objectives:** Genetic variants in susceptibility genes were reported to influence the pathophysiology of traumatic brain injury (TBI). Tumour necrosis factor-a (TNF-a), a proinflammatory cytokine, is induced shortly after TBI. TNF-a expression levels were correlated with the extent of brain tissue injury and with the clinical outcome. Allele A carriers of TNF-a (-308) gene polymorphism were found to have higher levels of TNF-a. We conducted a prospective clinical study to test possible influence of TNF-a (-308) gene polymorphism on patients’ clinical presentation and 6 month outcome after TBI.

**Methods:** 216 patients with TBI (mean age±SD=39.8±21.1, females=35 (16.2%]) successively admitted to the neurosurgical unit were evaluated. Initial neurological status was assessed by means of the Glasgow Coma Score (GCS), while we defined patients’ six-month outcome using the Glasgow Outcome Scale (GOS). We genotype for IL-6 (-174) polymorphism from blood samples using standard PCR/RFLP method. Possible associations were examined using the t-test, the Fisher’s exact test and the x2 test. Odds ratios with the corresponding 95% confidence intervals were also calculated using logistic regression analysis.

**Results:** The population was in H-W equilibrium. Distribution of TNF-a genotypes and alleles were similar in TBI patients with favourable (GG=77.9%, GA=21.5%, AA=0.6%, G=88.7, A=11.3) and unfavourable (GG=76.7%, GA=20%, AA=3.3%, G=86.6%, A=13.4%) outcome. (p=non-significant). There was also no significant influence of TNF-a polymorphism on patients’ GCS at admission (p=non-significant).

**Conclusion:** Our study fails to provide evidence of an implication of TNF-a (-308) gene polymorphism in the patients’ clinical presentation at admission and 6 month outcome after TBI.

**P2313**

**INTERLEUKIN 1A (-889) GENE POLYMORPHISM AND PRIMARY INTRACEREBRAL HEMORRHAGE**

E. Dardiotis3, M. Dardioti3, A. Komnos1, K. Paterekis2, A. Tasiou2, K. Aggelakis1, G. Xiromerisiou1, J. Gabranis4, A. Papadimitriou1, G.M. Hadjigeorgiou1

1Department of Neurology, University Hospital of Larissa, 2Department of Neurosurgery, University Hospital of Larissa, University of Thessali, 3Intensive Care Unit, 4Department of Pathology, General Hospital of Larissa, Greece

**Objectives:** Cerebral amyloid angiopathy and apolipoprotein E gene polymorphism have been implicated in the pathogenesis of intracerebral haemorrhage (ICH). Inflammatory cytokines seem to play an important role in the pathogenesis of the vascular wall. Interleukin-1a (IL-1a) gene polymorphism was associated with ischemic stroke and Alzheimer’s disease. We conducted a prospective study to test possible association of IL-1a (-889) gene polymorphism with ICH.

**Methods:** 147 prospectively recruited patients (mean age±SD=63.5±14.2; females 31.1%) with ICH and 215 age- and gender-
matched control subjects were genotyped for the IL-1a (-889) gene polymorphism. The following data were collected: age, gender and other epidemiological factors, location and volume of ICH, Glasgow Coma Scale (GCS) at admission and 6-month modified Rankin Scale (mRS). H-W equilibrium was tested with exact test. Odds ratios (ORs) and corresponding 95% coefficient intervals (CI) were calculated using logistic regression. Possible association was examined using the Fisher’s exact test. 

Results: The population was in H-W equilibrium. The distribution of the IL-1a genotypes in the whole group of ICH patients (CC=42.6, CT=40.8, TT=13.0), in patients with lobar ICH (CC=46.9, CT=42.9, TT=10.2) and non-lobar ICH (CC=45.9, CT=39.8, TT=14.3) did not differ from that of the controls (CC=49.8, CT=39.1, TT=11.1) (p=non-significant).

Conclusion: Our study did not provide evidence of an implication of IL-1a (-889) gene polymorphism in the development of ICH.

P2314
A MULTIDISCIPLINARY TEAM APPROACH TO SCREENING CHILDREN FOR DEVELOPMENTAL DELAY – PRELIMINARY FINDINGS USING THE DIAGNOSTIC INVENTORY FOR SCREENING CHILDREN (DISC) IN THE BAHAMAS
E.L. Demeritte, L.B. Colaco, D. May, A. Hanna
Department of Paediatrics, The Neurodevelopmental Clinic, The Princess Margaret Hospital, Nassau, Bahamas

Background: Current research states that developmental delay occurs in up to 15% of the children below 5 years old. Local information is currently anecdotal. An early intervention clinic was recently established for children at risk or with developmental delay. It is unique to the Caribbean and serves as a catchment centre for the entire Bahamas. Preliminary findings from this study will shed some light on the prevalence of developmental delay locally and also assist in the provision of their care.

Method: A list of children screened with the DISC at baseline in 2005 was compiled. The charts of these children were then reviewed and pertinent information was abstracted onto a form which was subsequently entered and analyzed using SPSS version 11.5.

Results: n=54. M: F=1:0.69. The mean age of children at baseline screen was 14.5 months (3.71, 25.49), range = 2.3 months – 58 months. The mean birth weight was 3.54 lbs (1.6, 5.48). Approximately 74% (n=40) were labelled as abnormal in 2 or more domains.

Conclusion: According to the DISC results, there is evidence of developmental delay in children at baseline screening. Provisions for adequate resources such as therapists, workspace, and equipment may have to be made, to accommodate this population needs. Further study at all other health care facilities is warranted for a population-based prevalence study.

P2315
A CASE OF OVARIOLEUKODYSTROPHY WITHOUT EIF2B MUTATIONS
C. Gaudiano, C. Di Perri, O. Scali, A. Rufa, C. Battisti, N. De Stefano, A. Federico
Department of Neurological and Behavioural Sciences, University of Siena, Italy

Vanishing white matter (VWM) disease, also known as childhood ataxia with central nervous system hypomyelination (CACH) syndrome, is an autosomal recessive leukoencephalopathy, first described by Schiffman et al. in the 90s, related to mutations in each of the 5 genes (EIF2B1,2,3,4,5) encoding for the 5 subunit of eukaryotic translation initiation factor 2B (EIF2B0,β,γ,δ,ε), essential for protein synthesis. The phenotypic variation is extremely wide, disease onset occurs usually in childhood, with progressive neurological deterioration characterized by ataxia, spasticity and variable optic atrophy. A new association of Vanishing White Matter (VWM) and Premature Ovarian Failure (POF) was recently described as a sole entity called ovarioleukodystrophy. The condition was found to be related to mutations in the EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5 genes, the same were responsible for the VWM disease, suggesting a common pathophysiological mechanism. We describe the case of a young patient (32 y.o.) with premature ovarian failure (POF) and leukodystrophy (LD) of unknown cause (ovarioleukodystrophy), not carrying any EIF2B mutation. She developed neurological (dysphagia, anarthria, tetraparesis) and cognitive impairment, ovarian failure and her MRI scan showed diffuse and bilateral leukodystrophy. It suggests the possibility that different genes, beside the known ones, might be involved in the protein synthesis causing myelin disorders in the ovarioleukodystrophy.

P2316
NEUROPSYCHOLOGICAL ABILITIES IN CHILDREN WITH APRAXIA OF SPEECH
V. Djordjevic1, S. Golubovic2
1Institute for Experimental Phonetic and Speech Pathology, 2Faculty of Special Education and Rehabilitation, University of Belgrade, Serbia

Developmental apraxia of speech is a severe deficit in the ability to volitionally program speech movements. This disorder has a neurogenic etiology, but evidence of brain damage or dysfunction has not been consistently demonstrated in children diagnosed as having DAS on the basis of widely varying criteria. We researched neurological, intellectual abilities and intelligibility of speech in 15 children with apraxia of speech, 15 with developmental dysphasia and 15 with dysarthria. All 15 children with dysarthria and all 15 children with developmental dysphasia had regular neurological findings, while all 15 children with apraxia of speech had positive neurological findings, which is different from findings of other researchers. Children with apraxia of speech (IQ100) had the lowest IQ, then children with developmental dysphasia (IQ102) and children with dysarthria (IQ110). According to affirmed IQ between developmental dysphasia and apraxia of speech there is no statistically important difference (P0.05), while there is statistically important difference between dysarthria and dysphasia (p<0.05). In our research, DAS children typically demonstrate performance scores at least 10 points higher than verbal scores on tests of intelligence due to their reduced expressive language facility. Test of intelligence should be viewed as a single measure; additional testing as the child matures may be necessary before a decision regarding reduced verbal compared to performance abilities can reliably be made. Ineligibility of speech was reduced due to frequently omitted motorically complex speech sounds, vowel distortions, variable productions of the same word, and the combining of multi-word utterances into a single word.

P2317
SPINOCEREBELLAR ATAXIA TYPE 6 PRESENTING IN INFANCY
J.A. Gosalakkal
University Hospitals of Leicester, Leicestershire, UK

SCA6 is one of the several hereditary progressive cerebellar ataxias first described in 1997. Genetic studies have identified the defect as abnormal expansion of CAG trinucleotide repeat in
1 alpha subunit of calcium channel gene located on chromosome 19p13. The symptomatic individuals have 20 to 33 repeats in contrast to normal population who show 19 or less CAG repeats. Most of the earlier reports show the age of onset of symptoms to be after the 3rd decade. We present a patient with episodic symptoms soon after birth, which is unusual, and to our knowledge, is the youngest reported case. The clinical features of SCA type 6 are variable. In this case report we discuss the mode of inheritance and the common symptoms of this condition.

P2318
THE USE OF INTERFERON BETA IN CHILDREN WITH MULTIPLE SCLEROSIS
H. Ben Rhouma, I. Ben Youssef-Turki, A. Rouissi, N. Gouider-Khouja
Department of Paediatric Neurology, National Institute of Neurology, Rabta, Tunis, Tunisia

Introduction: Multiple sclerosis (MS) in childhood is rare. Interferon Beta (INF B) was recently used to treat children with relapsing-remitting MS. We report 5 patients with MS: 4 of them were treated by INF B1a. The primary goal of this study is to summarise clinical presentation, diagnosis and treatment characteristics in paediatric MS.

Cases reports: 4 girls and 1 boy had a relapsing-remitting course (mean age 14.4 years). Mean age of onset was 11.4 years. Mean presenting symptom was motor weakness; physical exam showed motor weakness, sensory disturbance, bulbar symptoms, cognitive disturbance and sphincter dysfunction. Diagnostic tests included Magnetic Resonance Imaging (MRI), evoked potentials and cerebrospinal fluid exam. All patients received methylprednisolone pulse therapy when relapse occurred. The median Expanded Disability Score Scale (EDSS) was 4 before pulses and 3.75 after. 4 patients were treated by INF B1a; all patients used paracetamol before treatment to prevent pseudo-flu syndrome. The starting dose of INF Beta (INF B) was recently used to treat children with relapsing-remitting MS. We report 5 patients with MS: 4 of them were treated by INF B1a. The primary goal of this study is to summarise clinical presentation, diagnosis and treatment characteristics in paediatric MS.

Discussion: Therapy in adults with MS is to initiate INFβ early in the course of the relapsing-remitting form of the disease. We believe this is also applicable in children. Large randomised trials of INFβ in paediatric MS are necessary to confirm its efficacy and safety in children.

P2319
EEG IN CHILDREN WITH PERINATAL HYPOXIC-ISCHAEMICENCEPHALOPATHY (PHIE) WHO DEVELOP EPILEPTIC DISCHARGES
A. Hadjiu¹, S. Hadjiu², I. Iliciuc³, C. Călciu⁴
¹Department of Neuro-Paediatrics, The State University of Medicine and Pharmacy “Nicolae Testemitanu”, Chisinau, Moldova

Background: EEG contributes in the diagnosis of post-ischaemic discharges, has diagnostic and prognostic value and is the indicator of a child’s psycho-neurological development.

Methods: The study consisted of 165 patients with PHIE (age: from 2 weeks to 6 months) who developed epileptic discharges. EEG was made before and after the discharge. The comparison lot consisted of 65 children without discharges.

Results: Epileptic discharges developed in medium PHIE’s form (27%), normal EEG findings were found in 87%, severe EEG’s route (78%), profound abnormal stroke (78%). The suppression’s level and duration correlating with PHIE’s stringency generated a big risk of epilepsy’s development (45%). The suppressions-burst were found in 34% of children with precocious discharges, in comparison with the control group 4.8%, inactive strokes – in 27%, in comparison with 3.2%. The severe prognostic is suggested by inactive stroke, suppression-burst patterns more than 2 weeks. Periodical focal discharges were registered in 4%, in comparison 1.3%, were followed by reserved prognostic. Delta intermittent activity was seen in 27% after discharge, which was followed by undue epilepsies. Normal EEG 54.5%, but without discharges, in comparison with 6.4% from those with discharges.

Conclusions: Normal strokes with weak reactivity are frequent in medium form PHIE. The EEG’s prognostic value is maximal in the first days of the life, the persistence of EEG’s anomalies 2 weeks after, in children with PHIE it represents an indicator of severe prognostic for an unfavourable neurological evolution in all the cases.

P2320
DUPLICATION OF MECP2 IN A GIRL WITH RETT SYNDROME VARIANT
A. Jansen¹, M. De Rademaeker², L. De Meirleir¹, S. Seneca²
¹Department of Paediatric Neurology, ²Department of Medical Genetics, University Hospital Brussels, Belgium

Objective: To report a duplication of the MECP2 gene as a possible cause of forme fruste Rett syndrome (RTT) variant.

Methods: The proband was examined, and medical and family histories were obtained. Brain MRI, as well as genetic studies including karyotype, subtelomere FISH, FISH for deletion 22q11, and screening for fragile X and Rett syndrome, were performed.

Results: A 13-year-old girl presented with mild mental retardation. She was the only child of consanguineous parents. Early developmental milestones were normal. She attended a regular kindergarten, but was transferred to special education at age 5.5 years. At age 13 years, she is well oriented and has normal speech. Gait, balance, coordination and deep tendon reflexes are normal. She has occasional hand-washing movements and a discrete tremor of both hands. Full Scale IQ score was 63. MRI of the brain was normal. Analysis of the MECP2 region by MLPA techniques showed a de novo duplication of the MECP2 gene. X-inactivation studies in the proband and her mother were not informative.

Conclusions: The finding of a duplication of MECP2 in a girl with forme fruste RTT underlines the importance of quantitative analysis of MECP2 in patients with variant RTT without point mutations. Duplications affecting the Xq28 region have been reported in 2 girls with classical RTT, 1 with preserved speech variant RTT, and 1 with RTT not specified. Duplications involving MECP2 have also been reported in males with severe mental retardation and progressive neurological symptoms.

P2321
THE METHYLENETERAHYDROFOLATE REDUCTASE GENE C677T POLYMORPHISM AND RISK OF VASCULAR DISEASES – PRELIMINARY RESULTS
K. Jastrzębski, J. Zagorski, A. Klimek
Department of Neurology and Epileptology, 2nd Department of Neurological Diseases, Medical University of Lodz, Poland

Background: The methylenetetrahydrofolate reductase (MTHFR) is a critical enzyme involved in the metabolism of folates and methionine. It catalyses the reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, thus generating the active...
form of folate required for remethylation of homocysteine to methionine. Patients with homozygous 677C>T common variant of MTHFR gene have impaired homocysteine metabolism and elevated blood homocysteine levels. Hyperhomocysteinemia has been reported as a risk factor of atherosclerosis. It was proposed that the MTHFR gene C677T polymorphism can influence the homocysteine concentration on cellular level without elevated plasma homocysteine concentration what might be involved in the higher risk of atherosclerosis and vascular diseases.

Materials and methods: To investigate the role of genetic predisposition in vascular diseases we analysed MTHFR genotype on DNA from patients after stroke and myocardial infarction by means of PCR-restriction fragment length polymorphism analysis. To this time we have examined 85 participants with stroke (15, group I), myocardial infarction (30, group II) and without vascular diseases (40 control group III).

Results: We want to present our preliminary results.

Key Words: Methylene tetrahydrofolate reductase, Polymorphism, Homocysteine, Vascular diseases.

P2322

STUDY DESIGN IN INVESTIGATOR-INITIATED PHASE III CLINICAL TRIAL OF L-ARGININE ON MELAS

Y. Koga, Y. Akita, J. Nishioka, S. Yatsuga, K. Katayama,
T. Matsuishi
Department of Paediatrics and Child Health, Kurume University School of Medicine, Kurume, Fukuoka, Japan

Objective: In order to monitor and to evaluate the efficacy of drugs to prevent the progression of disease and/or cure the stroke like episodes in MELAS, we have to create the multi-dimensional, semi-quantitative, and reproducible clinical rating scale which is suitable for clinical trial in MELAS.

Background: MELAS is a maternally inherited multisystem disorder characterized by early onset stroke like episodes. However there is no clinical rating scale to monitor the severity or progression of the disease, and no validated endpoints to evaluate the efficacy of drugs on MELAS. Since MELAS shows diverse clinical pictures in any ages ranging from childhood to adult, we have to establish the clinical rating scale to specify the evaluation of efficacy of therapeutic drugs of this disease.

Design and method: We have created and evaluated patients by the MELAS Stroke scales, Japanese Mitochondrial rating scale (JMRS), MIDAS (migraine disability Score), and Time to the first event during disease progression. Then we established the study design for Phase III clinical trial of L-arginine on MELAS which has been approved by PMDA (Pharmaceutical and Medical Devices Agency) in Japan.

Results and discussion: JMRS, MELAS stroke scale, MIDAS and time to the first event is useful for monitoring the disease progress in MELAS, multi-dimensionally, semi-quantitatively, and reproducibly. Above shown scales will be a powerful tool to evaluate the longitudinal clinical course and evaluate the efficacy of therapeutic intervention of L-arginine on MELAS.

P2324

PROMOTER OF THE CD14 MONOCYTE RECEPTOR GENE AND LEVODOPA-INDUCED ADVERSE EFFECTS IN LEVODOPA-TREATED PARKINSON’S DISEASE

J.J. Lin1,2, K.C. Yuch1
1Department of Neurology, Chushang Show-Chwan Hospital, Nantou, 2Department of Neurology, Chung-Shan Hospital, Taipei, Taiwan-R.O.C.

Background and aims: Recent studies have emphasized that genetic factors may involve the occurrence of the adverse effects of chronic levodopa therapy in PD patients. The promoter of the CD14 monocyte receptor gene (pCD14) was proved to confer a genetic susceptibility for the risk of PD. This study was designed to assess whether the genetic polymorphism could be a predictor of levodopa-induced adverse effects in PD.

Method: This study included 195 chronic levodopa treated PD patients and their mean age at onset of PD was 64.2±10.8 years. The duration of disease and the treatment with levodopa was 6.6±4.8 and 5.5±4.0 years, respectively. The levodopa-induced adverse effects included dyskinesia, “on-off”/“wearing off” phenomena and psychosis.

Results: The frequency of the TT genotype of the pCD14 polymorphism (pCD14-TT) in PD patients with levodopa-induced “on-off”/“wearing off” was significantly higher than that in PD patients without the adverse effect (p=0.048), but the genetic polymorphism was not associated with the risk to develop dyskinesia or psychosis induced by levodopa. A logistic regression analysis confirmed that the pCD14-TT genotype was an independent risk factor for levodopa-induced “on-off”/“wearing off” in PD patients (OR=1.462, p=0.041).

Conclusion: Results of the study showed that pCD14-TT genotype might confer a primary predictor for the occurrence of “on-off”/“wearing off” in levodopa-treated PD.

P2323

ANALYSIS OF CORTICOSPINAL PATHWAY FUNCTION IN CHILDREN WITH PERIVENTRICULAR LEUCOMALACIA EVALUATED BY MOTOR EVOKED POTENTIALS

C.G. León Castillo
Unidad de Investigacion de Neurodesarrollo, Instituto de Neurobiología, Juriquilla Queretaro, México

Objective: The aim of this study was to compare the motor evoked potentials (MEP) by Transcranial Magnetic Stimulation (TMS) in babies with Periventricular leukomalacia (PVL) and healthy babies.

Material and methods: We examined 18 babies with PVL and 9 controls with a mean age of 3 months. The MEP was obtained with TMS of motor cortex and spinal cord at cervical and lumbar levels. The registering of MEP was in the abductor pollicis brevis (APB) and the tibialis anterior (TA). We evaluated for each MEP, latency, duration, amplitude, central (CCV) and peripheral (PCV) conduction velocity.

Results: In the PVL group, the MEPs of right APB had a latency of 30.78 ms, amplitude of 182.84 mV, duration of 10.55 ms, CCV of 9.48 m/s and CPV of 24.28 m/s. In the right TA the latency was of 31.05 ms, amplitude of 182.85 mV, duration of 13.56 ms, CCV of 17.96 m/s and CPV of 20.46 m/s. A significant difference with control group was found in latency (p=0.0009) and CCV (p=0.004).

Conclusions: We concluded that the LMP modifies the conduction of the corticospinal pathway, showing a significant increase of the latency and a decrease of the CCV in babies with PVL. The MEP by TMS can be a useful technique for the early diagnosis of LMP.
P2325
A NOVEL (CYS391ARG) PSEN2 MUTATION IN A PATIENT WITH SPORADIC EARLY ONSET ALZHEIMER’S DISEASE
1Department of Neurology, UH, 2Laboratory of Molecular Pathology, Medical University, Sofia, Bulgaria, 3Molecular Genetics Department, University of Antwerp, Belgium

Background: Alzheimer’s disease (AD) is the most common cause of dementia and may be present in familial and sporadic forms. Mutations in 3 genes – amyloid precursor protein (APP), Presenilin 1 (PSEN1), and Presenilin 2 (PSEN2) – are associated with early onset AD.

Methods: We studied the phenotype of a Bulgarian AD patient with PSEN2 mutation. DNA sequencing of PSEN2 and detailed clinical, neuropsychological, and neuroimaging examinations were performed.

Results: The proband is a 62-year-old teacher with no family history of neurological disease. The initial symptoms at age 54 were difficulties in maintaining concentration and mild memory disturbances, not affecting activities of daily living. The first neuropsychological evaluation at the age of 56 showed impairment of short-term and episodic memory, without other cognitive deficits, thus suggesting the diagnosis of mild cognitive impairment (MCI). Upon re-examination a year later the psychometric testing showed orientation and executive function deficits. A CT scan revealed bi-temporal lobar atrophy. An initial diagnosis of probable AD was suggested. At 60 years of age the patient was still working as a teacher (MMSE=26). The brain MRI revealed marked cortical atrophy and white matter changes. The last neuropsychological examination documented mild to moderate dementia (MMSE=18) at 62 years.

Conclusions: We identified de novo PSEN2 (Cys391Arg) mutation in a patient with sporadic AD. There are several reports of patients with PSEN2 mutations clinically characterized by long-term progression. Similarly, our patient had a clinical course of MCI for 3 years, before the development of dementia, which suggest long disease duration.

P2326
ADHD IN CHILDREN: CO-MORBIDITY WITH SLEEP DISORDERS
A. Michopoulou, B. Belesioti, V. Goula, K. Pantazopoulou, X. Tokatlidou, O. Papazani, M. Savvidou
Department of Psychology, General Children’s Hospital of Penteli, Palaia Penteli, Athens, Greece

Objectives: Parents, consulting the Psychology Department of the General Children’s Hospital of Penteli about their children’s concentrating difficulties, often complain that they also have sleep problems. The aim of the present study is to examine the co-morbidity between ADHD and sleep disorders.

Methods: The study consisted of 173 children, who consulted the Department about the above problems, aged 6 to 14 (68.2% boys, 31.8% girls). Children were categorized into two groups: a) children diagnosed with ADHD b) children not diagnosed with ADHD. Parents were invited to complete the ADHD-IV scale, as well as the Aschenbach CBCL test. Children were submitted to BECK’s Youth Inventory. In order to compare the two groups, we used t-test.

Results: Considering the parents’ and children’s reports, it was found that co-morbidity between ADHD and sleeping difficulties does exist to a significant level. More precisely, children with hyperactivity, compulsiveness and concentrating difficulties also seemed to experience low quality of sleep. Co-morbidity between ADHD and sleep disorders was not found to be affected by sex, whereas age seemed to be an important factor.

Conclusions: A considerable percentage of children diagnosed with ADHD was found to have significant sleep disorders. It is also important to note that children, presenting not the whole syndrome but some symptoms of ADHD, also tend to have sleep difficulties.

P2327
CLINICAL DIVERSITY AND MRT DIAGNOSIS OF X-COUPLED ADRENOLEUKODYSTROPHY (X-ALD)
T. I. Muravina1, S. V. Serkov1, O. V. Bykova1, E. Yu. Zakharova1, S. N. Illarioshkin2, V. N. Kornienko2
1Institute of Neurology, RAMS, 2Institute of Neurosurgery, RAMS, 3Scientific Centre of Children’s Health, RAMS, 4Medicogenetic Scientific Centre, RAMS, Moscow, Russia

X-ALD is a peroxysome disease and is characterized by a damage of the nervous system. Demyelination of the white matter is related to a disorder of the structure and incorporation into myelin of long-chain fatty acids. The preliminary diagnosis was verified biochemically or by molecular genetics methods. In the clinical structure dominate children’s and juvenile cerebral forms. The possibilities of MRT in diagnosis of X-ALD were evaluated. 10 patients aged from 5 to 24 years were examined. The brain was studied by diffused weighted MRT, proton MR-spectroscopy. In 2 cases MRT of the spinal cord was performed. The characteristic signs were revealed in all patients: a diffuse symmetrical damage of the corpus callosum torus and deep periventricular white matter changes of the parietooccipital areas with involvement of the visual radiations, corticospinal tracts on both sides, including the region along the whole spinal cord. In one case, the vector of damage was inverted in occipitofrontal direction. In another case, a combined damage of both the torus and knee of the corpus callosum at its intact body, was noted. In all cases was noted a pathologic contrasting of the demarcation zone of demyelination, that is not encountered in other leukodystrophies. Spectroscopy showed a pathologic lipid-lactate complex in the areas of damage, reduction of NAA and increase of Cho/Cr ratio, that is the sign of demyelination of the white matter. DW-MRT revealed a significant increase of diffusion in the affected areas (destruction of myelin and axons).

P2328
FEBRILE MYOCLONUS – A GENERAL PAEDIATRIC VIEW
T.S. Nedungadi, N. Prakash, U. Varma
Department of Paediatrics, Royal Oldham Hospital, Oldham, Lancashire, UK

Febrile convulsion is the most common seizure disorder during childhood with a uniformly excellent prognosis. They are typically generalised tonic clonic. The convulsion may present rarely as myoclonus. Febrile myoclonus is a rare condition which is benign and resolves with resolution of fever and does not warrant intervention. Here we present a case of febrile myoclonus in view of rarity of the condition and also because of the frequency of episodes. General paediatricians need to be aware of this benign condition. A 20-month-old child presented with febrile fits on the background of diarrhoea and vomiting. He had further 2 witnessed episodes of myoclonic jerks while in the ward. There were no concerns regarding his development. Apart from his mother having
febrile convulsions as a child there was no other significant history of note. During these episodes he was febrile and alert. His systemic examination and investigations were normal. He presented 2 months later with fever and similar myoclonic jerky episodes secondary to an upper respiratory tract infection. An EEG was arranged which was normal. He is being reviewed as outpatient and there have been no concerns. So far evidence suggests that these children do well. Recurrence of the same is documented. It is important to be aware of this condition to allay anxiety for the family as well as for the practitioners. Febrile myoclonus is a recently recognised clinical entity with very few reported cases in literature.

P2329  
SURVIVAL OF DIFFERENT POPULATIONS OF DRG NEURONS AFTER SCIATIC NERVE INJURY OF BABY RATS
M.V. Nigmatzyanova, I.S. Rasinov, Yu.A Chelyshev  
Histology, Cytology and Embryology Department, Kazan State Medical University, Kazan, Russia

The DRG neurons differ in their functional properties, sensitivity to neurotrophins and neurotrophic factors. Small size neurons are responsible to the pain and thermoesthesia, medium size neurons – to the tactile sensitivity and large neurons – to the proprioception. In our previous study we have shown that the total number of neurons increased from P0 to P30 day in postnatal development of rat’s pups, also we found modification of percent correlation between different populations. In the current study we estimated the total number of L5 DRG sensory neurons, quantity of the small, medium and large neurons populations on post-natal day 15 and 30, with previous injury of sciatic nerve of newborn pups (P0). The total number of neurons on P15, after injury decreased by 40% (p<0.05), at the same time the number of small and medium neurons decreased by 44% (p<0.05) and 60% (p<0.05), the number of large neurons remained unchanged. On P30 after injury the total number of neurons unchanged with P15+injury, but decreased by 49% (p<0.05) with intact P30 pups. The number of small neurons increased by 46% (p<0.05), and the number of large and medium neurons decreased by 31% (p<0.05) and 18% (p<0.05), accordingly with P15+injury. The large and medium neurons death with more value than small neurons after sciatic nerve injury of P0 baby rats.

P2330  
A CASE REPORT OF HEREDITARY SPASTIC PARAPLEGIA WITH THIN CORPUS CALLOSUM
S. Ozakbas, O. Sahin  
Department of Neurology, Dokuz Eylul University, Izmir, Turkey

Background and aims: Hereditary spastic paraplegia with thin corpus callosum (HSP-TCC) is characterized by slowly progressive spastic paraparesis and mental retardation with normal motor development, and extremely thin corpus callosum. It was thought to be essentially a Japanese subtype of HSP. Only 17 white families with HSP-TCC have been reported so far. Muscular atrophy, extrapyramidal symptoms, cerebellar ataxia and epileptic seizures may occur especially often late in the progression. Here we report the case of a 21-year-old female with HSP-TCC.

Case report: She presented a 9-year history of frequent falls, gait disturbance, progressive muscular weakness, and pain in the lower limbs. She had normal achievement of motor milestones. There was no family history and her parents were unrelated. General physical examination was normal. On neurological examination, she presented mild dystarhria, bilateral hemiparesis more marked in her lower limbs, four sided spasticity, bilateral Babinski sign and spastic gait. All biochemical, haematological, and endocrine tests were normal. Needle electromyography, nerve conduction studies and electroencephalogram were also normal. A somatosensory evoked potential study, revealed bilateral fasciculus gracilis involvement. In brain magnetic resonance imaging, the corpus callosum was extremely thin. Her mental examination accorded with mental retardation (verbal IQ: 63 points, performance IQ: 57 point and total IQ: 59 points).

Conclusion: To our knowledge, there were only 17 Caucasian families with HSP-TCC described. Herein, we described the first Turkish patient with the typical clinical and radiological features of HSP-TCC.

P2331  
ANALYSIS OF HEADACHE IN CEREBRAL VASCULAR DISEASES IN CHILDREN. CLINICAL AND NEURO-RADIOLOGICAL CORRELATION
E. Pilarska, M. Lemka, K. Reclawowicz  
Department of Developmental Neurology and Neurology, Medical University of Gdansk, Poland

Background: Headache in cerebral vascular diseases, especially in adults occurs quite often, whereas their frequency differ in connection with the kind of vascular disease, its etiology, the localization of the changes. There are only a few researches connected with this problem in children. Aim of the study – the analysis of headache in cerebral vascular diseases – in ischemic and haemorrhagic strokes was provided.

Material and method: The analyzed group included 30 children aged 5–16 years with ischemic or haemorrhagic stroke diagnosed by investigation, clinical symptoms and confirmed by CT, MRI, angio MRI, AEG, who were treated within the Department of Developmental Neurology Medical University of Gdansk within the years 2002–2006. The severity of headache at the onset of the disease, its localization, other symptoms and changes with neuro-radiological examinations were analyzed. The characteristic of previous headache before the stroke was made.

Results: Only in 1/4 of the patients we observed the headaches before the acute stage of the disease. Nobody presented migraineous headache. Headaches occur more often in haemorrhagic stroke (80%) than in ischemic (40%). In the majority of children the chronic headache after the stroke has not been noticed. The significant correlation between the localization of both stroke and headache was not found.

Conclusion: Headaches can be treated as a first, dangerous symptom in cerebral vascular diseases, but these observed before the acute stage of the disease usually do not have any connection with vascular diseases in children.

P2332  
PIRACETAM TREATMENT IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER
G.S. Pilina  
Neurology Department, Paediatric Regional Clinical Hospital, Izhevsk City, Udmurtia, Russia

Attention Deficit Hyperactivity Disorder (ADHD) is the most common learning dysfunction among children. The primary
symptoms of ADHD include regulation attention difficulties, distractibility, impulsivity and hyperactivity. Psychostimulants, anti-depressants and neuroleptics are usually used in therapy of children with ADHD. This treatment diminishes motor activity, but lowers cognitive functions; also children have to take medicine for a long time. Hereby, new therapy ways are a very urgent and a timely problem. We studied the effectiveness of Piracetam in the treatment of children with ADHD.

Methods: The study sample consisted of 14 children with ADHD, ranging in age from 7 to 10 (main age 8.2±0.61). The investigation included neurology status, Shulte test and computer EEG with spectral and coherence analysis. Children were examined before and after treatment. The therapy consists of 1 month treatment with piracetam; the treatment dose was 1600 mg per day twice daily.

Results: In dynamics, attention characteristics improved with 12 (85.7%) (p<0.01) and the power of alpha rhythm became higher in EEG spectrograms with 10 (71.4%) (p<0.01) children. All children became less hyperactive and impulsive at the end of treatment. Coherence analysis shows normalization of level of relations between brain hemispheres in central and parietal parts among 14 children. There were not detected any side-effects, in children during piracetam treatment.

Conclusion: The effectiveness of piracetam in treatment of children with ADHD can objectively be seen from the results of the study. Also it should be taken into consideration that all children showed well tolerability of the treatment.

P2333
AUTO-IMMUNE MYASTHENIA GRAVIS IN CHILDREN
E. Santos1, M. Santos2, A. Martins da Silva3
1Neurology Department, Hospital Geral Santo Antonio, 2Neurology Department, Hospital Especializado Em Criançãs Maria Pia, Porto, Portugal

Introduction: Myasthenia gravis in childhood is rare, comprising 10% of all patients. Diagnosis is made on clinical and neurophysiological basis. Serum acetylcholine receptor antibodies (AchRAb) are more frequently negative than in adults. Treatment options are based in small series and with concern over long-term effects in early ages of steroids, immunosuppressants and thymectomy.

Objective: To describe clinical course of all patients with the diagnosis of MG, in childhood or adolescence, attending Neuromuscular and Neuroimmunology centres in two Oporto tertiary hospitals.

Methods: Review of clinical records of above described patients, during the period 1986–2006.

Results: 7 patients, 6 are girls. Current ages are 9–35y. Initial symptoms started in pre-puberty in 2 (3 and 7y), and after puberty in 5 (12–15y). None had a family history. Presentation symptoms were oculo-bulbar, except in one with proximal limb weakness. Finally all were diagnosed as MG. First EMG showed decrement in repetitive stimulation >10% in 6. 4 were tested to serum AchRAb and were positive. They were treated initially with pyridostigmine. Then, 5 needed corticosteroids. After a mean follow-up of 13 years (2–22y), 1 is in spontaneous remission and 6 under medication. 2 only with pyridostigmine, 2 in association to Ig iv and steroids, 1 to mycophenolate mofetil and steroids and 1 to steroids. 5 underwent thymectomy (after 12y).

Discussion: These patients had classical symptoms, nonetheless diagnosis took at least, some months in all of them. Their characteristics were similar to the published data and a few doubts related to the proper age to thymectomy remained.

P2334
ASSOCIATION OF INTRANATAL BRAIN HYPOXIC INJURIES WITH DIFFERENT STAGES OF GLUTATHIONE-S-TRANSFERASES T1 AND M1 POLYMORPHISMS
N.P. Shabalov1, T.E. Ivachenko2, O.A. Shahmetova1
1Pediatric Department, Saint-Petersburg State Paediatric Medical Academy, 2Laboratory of Prenatal Diagnostics, Saint-Petersburg State Academy of Obstetrics and Gynaecology, Saint-Petersburg, Russia

Introduction: Hypoxic damage is one factor of neonatal diseases. This research is devoted to link between intranatal hypoxia influence glutathione-S-transferases T1 and M1 polymorphisms. Reactive oxygen species contributes to oxidative brain injury. The glutathione-S-transferases (GST) family and microsomal epoxidase-hydrolase enzymes detoxify reactive oxygen species. Our hypothesis is that decreasing of the activity of these enzymes is associated with hypoxic brain damage.

Purpose: The establishment of a connection between intranatal hypoxic injuries with different stages and glutathione-S-transferases T1 and M1 polymorphisms.

Methods: This study determined allelic distribution of these polymorphisms in a study of 100 intranatal hypoxic injuries and 100 controls.

Results: The study showed that frequency of genes with decreased functional activities (GST T1 0/0 and GST M1 0/0) was much higher in the basic group. In case of mild damage reliable difference was founded for GST T1 0/0 (p<0.036, X2 – 4.38), GST M1 0/0 (p<0.04, X2 – 4.08) and GST T1 0/0 / GST M1 0/0 (p<0.032, X2 – 4.59). In case of moderate injury difference was revealed for GST T1 0/0 (p<0.034, X2 – 4.52) and GST M1 0/0 (p<0.049, X2 – 3.58). In case of severe damage distinction was found for combination GST T1 0/0 / GST M1 0/0 (p<0.0058, X2 – 7.62).

Conclusions: This study suggests that hypoxic damage of the brain is associated with the presence of GST T1 0/0 and GST M1 0/0.

P2335
LISSENCEPHALY CORRELATION BETWEEN CLINICAL AND NEUROIMAGING FEATURES
R.I. Teleanu1, D.M. Teleanu2, F. Buruiana3, D. Vasile4, M. Mocanu5, D. Plasca6, D. Dragomir1
1Department of Paediatric Neurology, Dr. V. Gomoiu Children’s Hospital, 2Department of Neurosurgery, Emergency University Hospital, Bucharest, Romania

Introduction: Lissencephaly represents a severe malformation of neuronal migration characterized by the absence/reduction of cerebral circumvolutions. The cortex is abnormally thick on section; white substance is thin and appears as a “strip” around ventricles, sylvian fissures are oriented vertically. Subcortical band heterotopia is characterised by a gyral aspect almost normal or slightly pachygiric or superficial cortex and by the presence of a neurons strip located deep and separated from the superficial cortex by a layer of white substance.

Patients and methods: We studied 20 patients diagnosed with lissencephaly based on brain computed tomography or magnetic resonance imaging. 18 patients were classified as isolated lissencephaly, one had Miller-Dicker syndrome and one had subcortical band heterotopia.

Results and discussion: 15 patients experienced epileptic seizures with onset during the first year of life. The mental retardation
was present in all cases. 12 patients had early severe hypotonia followed by progressive hypotonia with developmental delay. The aim of this study is to underly the importance of neuroimaging techniques in recognition of this entity.

P2336
A RETROSPECTIVE AND PROSPECTIVE STUDY OF TUBEROUS SCLEROSIS IN CHILDHOOD
F. Burian1, A. Davitoiu2, R. Teleanu2, D. Plesca, I. Stancea, L. Cretu, M. Moieceanu, D. Dragomir
Paediatric and Paediatric Neurology Departments, Dr. V. Gomoiu Children’s Hospital, Bucharest, Romania

Background and aims: Tuberous sclerosis, a genetic disease inherited in an autosomal dominant manner, is part of the neurocutaneous syndromes. The present study aims to describe the clinical and imagistic characteristics in the evolution of tuberous sclerosis.

Materials and methods: From a total number of 16 986 patients with neurological problems admitted in our clinic from 1996 to 2005, the authors selected a group of 25 children with tuberous sclerosis. All cases were evaluated by clinical and neurological examination, EEG, imagistic assessments and psychometric evaluation.

Results: The authors compared the age at onset of the first clinical manifestations and the age when the diagnosis was established. They quantified the main clinical aspects. Cutaneous lesions were present in 96% of the patients (hypomelanic macule in 88%, facial angiofibroma in 36%, nail fibromas in 20%, Shagreen spots in 4%, frontal placards in 4%), while visceral lesions were present in 64% of the patients. 96% of the patients had neurological problems (various types of seizures, severe mental retardation, behaviour anomalies, sleep disturbances). Neuroimagistic assessments identified cerebral calcifications in 96% of the patients. Seizure-response to treatment was also evaluated.

Conclusions: The authors underline the various modalities of clinical presentation at the onset of the disease that could allow an early diagnosis and institution of the proper therapy. Tuberous sclerosis patient develop, in time, severe mental retardation, severe behaviour anomalies, motor deficits, organic seizures and visceral complications.

P2337
EPILEPSY AND EPILEPTIFORM ABNORMALITIES IN A POPULATION OF CHILDREN WITH AUTISM SPECTRUM DISORDERS
S. Duarte1, A. Duarte2, J.P. Monteiro2, L. Ventosa2, L. Lourenço2, M.J. Fonseca2, P. Breia2
1Neurology Department, 2Neuropediatrics and Development Unit, Hospital Garcia de Orta, Almada, Portugal

Object of Study: We aimed to analyse, retrospectively, the prevalence of seizures, epilepsy and EEG abnormalities in a population of autistic children and to describe their clinical and electroencephalographic features, therapeutic approach and outcome.

Method: The clinical files of 61 children with autistic spectrum disorder (DSM IV) were studied.

Results: Among the children investigated, 67% had an electroencephalographic evaluation (54% with sleep). The frequency of EEG abnormalities was 37% and focal paroxysms were the commonest finding, localized preferentially to frontal and temporal left regions. Epilepsy, diagnosed in 20% of our population, started early (from 2 months to 13 years; median: 12.5 months), and secondarily generalized seizures were the most frequent seizure type. Seizure control and EEG normalization were verified in most of the children treated with anticonvulsants, but the effects on behaviour and language were very variable. The subgroup with abnormal EEG had highest frequencies of epilepsy, regression, stereotypes and brain MRI abnormalities.

Conclusions: The highest frequency of epilepsy and abnormal EEG in this sample, when compared with general population, is in accordance with the already recognized association between epilepsy and autism. These children may represent a subgroup in which abnormal brain electric activity contributes to underlying pathophysiology.

Presence of early symptoms, regression or suspected seizures are factors that can favour the decision to request an electroencephalographic evaluation with sleep.

P2338
POSTNATAL DIAGNOSIS OF CONGENITAL HYDROCEPHALUS AND ASSOCIATED BRAIN ANOMALIES
D. Amrom1, S. Muaku1, I. Delpierre1, C. Christophe1
1Division of Paediatric Neurology, Department of Paediatrics, 1Department of Paediatrics, Hôpital Français, ULB, 1Department of Neuroimaging, Hôpital Universitaire des Enfants Reine Fabiola, Brussels, Belgium

P2339
CASE REPORT: KLIPPEL-FEIL SYNDROME WITH COLPOCEPHALY
E. Kalliolia1, M. Arnaoutoglou1, P. Pappa2, C. Karamanidis1, G. Xiromerisiou1, G.P. Spanos2, V. Kosta1, E. Avdelidou1, N. Arnaoutoglou1, S.J. Baloyannis1
11st Department of Neurology, AHEPA Hospital, Aristotle University of Thessaloniki, 2Eurodiagnosis Diagnostic Centre, Thessaloniki, Greece

P2340
IMMUNOLOGICAL DISORDERS IN EPILEPSIES OF THE FIRST YEAR OF LIFE
C. Calcii1, I. Ilciuc1, S. Hadjiu1, C. Turcan1
1Department of Child Neurology, Hospital of Mother and Child Health Care, Hospital of Psychiatry, Chisinau, Moldova

P2341
PREVENTION OF SELECTIVE NEUROPSYCHOLOGICAL DISORDERS IN HEALTHY CHILDREN AS A RECENT APPROACH IN PEDIATRIC NEUROLOGY
S. Fokina, Yu. Nechytaylo
Department of Developmental Paediatrics, Bukovinian State Medical University, Chernivtsi, Ukraine

P2342
SELECTIVE NEUROPSYCHOLOGICAL DISORDERS IN INFANTS AND TODDLERS AS EARLY MARKERS OF ATTENTION DEFICIT AND HYPERACTIVITY SYNDROME
S. Fokina, Yu. Nechytaylo, D. Nechytaylo, V. Bezruk
Department of Developmental Paediatrics, Bukovinian State Medical University, Chernivtsi, Ukraine

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
P2343
FREQUENCY OF DYSGRAPHY AND DYSORTHOGRAPHY IN CHILDREN AFTER WAR
J. Salic¹, S.M. Golubovic²
¹Center for Education and Rehabilitation Hearing and Speech, Banja Luka, Bosnia-Herzegovina, ²Faculty of Special Education and Rehabilitation, University of Belgrade, Serbia

P2344
CONTRIBUTION OF REEP1 GENE MUTATIONS TO HEREDITARY SPASTIC PARAPARESIS (HSP)
C.A.A. Hewamadduma¹, J. Kirby², C.J. McDermott³, A. Grierson¹, A. Dalton⁴, P.J. Shaw¹,²
¹Academic Neurology Unit, Medical School, University of Sheffield, ²Royal Hallamshire Hospital, ³Department of Molecular Genetics, Sheffield Childrens Hospital, Sheffield, UK

P2345
LACOSAMIDE, AN INVESTIGATIONAL ANTI-CONVULSANT, HAS A FAVORABLE PROFILE IN PRECLINICAL REPRODUCTIVE, DEVELOPMENTAL AND JUVENILE TOXICITY STUDIES
N. Krebsfaenger, T. Stoehr
Department PhTox, Schwarz Biosciences GmbH, Monheim, Germany

P2346
EFFECTIVENESS AND PORTABILITY OF LAMICITAL IN CHILDREN
L.B. Kuanova
Neurological Department, Regional Hospital, Almaty, Kazakhstan

P2347
SIMULTANEOUS OCCURRENCE OF CHARCOT-MARIE-TOOTH DISEASE TYPE 1A (CMT1A) AND NEUROFIBROMATOSIS TYPE 1 (NF1)
S.B. Kwon¹, S.G. Kim¹, B.O. Choi¹, S. Jung¹, S.S. Hong¹, S.H. Hwang¹
¹Department of Neurology, Hallym University College of Medicine, Kangnam Sacred Heart Hospital, ²Department of Radiology, SoonChunHyang University College of Medicine, SoonChunHyang University Hospital, Seoul, South Korea

P2348
NEONATAL SEIZURES WITH A GENESIS OF CORPUS CALLOSUM AND PYRIDOXINE DEPENDENCY
T.S. Nedungadi, B. Padmakumar, U. Varma
Department of Paediatrics, Royal Oldham Hospital, Oldham, Lancashire, UK

P2349
LACK OF ASSOCIATION BETWEEN +738T/C POLYMORPHISM OF THE NFKBIL1 GENE AND OPTIC NEURITIS IN MULTIPLE SCLEROSIS IN A POLISH POPULATION
M.K. Owecki¹, P. Kowal¹, M. Kaczmarek², J. Hoppe-Golebiewska³, E. Nikisch³, E. Tokarz-Kuczynksi³, R. Slomski¹, W. Kozubski¹
¹Department of Neurology, University of Medical Sciences, ²Institute of Human Genetics, Polish Academy of Sciences, ³Laboratory of Computer Science and Statistics Medical Academy, Poznan, Poland

P2350
X-LINKED ADULT ADRENOLEUKODYSTROPHY AND ADRENOMYELONEUROPATHY: REPORT OF TWO CASES AND IMPORTANCE OF DIFFERENTIAL DIAGNOSIS AND TREATMENT
N. Subutay Oztekin¹, M.F. Oztekin², G. Orhan³, F. Ak³
¹2nd Neurology Department, ²1st Neurology Department, SB Diskapi Education and Research Hospital, Ankara, Turkey

Motor neurone diseases;
Muscle and neuromuscular junction disease;
Peripheral nerve disorders

P2352
DIABETIC PAINFUL DISTAL SENSORY POLYNEUROPATHY IS PREDOMINANTLY OF SMALL-FIBER TYPE
J. Bednarik¹, E. Vlckova-Moravcova¹, L. Mlakova¹, J. Belobradkova², C. Sommer²
¹Department of Neurology, ²Diabetologic Centre, Department of Internal Medicine and Gastroenterology, Faculty Hospital and Medical Faculty, Masaryk University, Brno, Czech Republic.
³Department of Neurology, University of Würzburg, Germany

Aim: To assess the frequency and classification of small-fibre involvement (both sensory and autonomic) in diabetic painful distal sensory polyneuropathy.

Methods: A cohort of 30 patients with diabetes mellitus type 2 (DM 2) or impaired glucose tolerance suffering from neuropathic pain in their feet was evaluated using nerve conduction studies, autonomic tests, thermal quantitative sensory testing (T-QST) and skin biopsy. Both intra- and subepidermal nerve fibre densities were quantified in skin punch biopsies immunostained for the PGP 9.5 antigen.
Results: Sensory signs of small-fibre involvement were present in 23 patients (77%), 7 patients had isolated positive sensory symptoms. Abnormalities in both skin biopsy and T-QST were present in 27 cases (90%). The remaining 3 cases displayed either abnormal skin biopsy or T-QST findings. 10 patients had concomitant electrophysiological or clinical signs of sensory large-fibre involvement. Autonomic dysfunction was found in 43.3% of the cases.

Conclusions: T-QST and skin biopsy are complementary in the detection of small-fibre involvement in diabetic patients and should optimally be included in diagnostic algorithms of these patients, especially in research conditions. Small- and large-fibre involvement frequency coincides in distal sensory diabetic polyneuropathy. Small-fibre involvement seems to serve as a prerequisite for and as an initial event in development of neuropathic pain in diabetics, but the exact patterns of evolution of pain through its various stages remain to be disclosed.

Acknowledgement: The study was supported by the Research Plan MSM0021622404 and by a grant of the ENS to E.V.M.

P2353

MOTOR CORTEX HYPEREXCITABILITY IN AMYOTROPHIC LATERAL SCLEROSIS
L.F. Bolokadze, I.F. Fedotova
Department of Neurology, Academy of Medical Science, Kharkov, Ukraine

Objectives: Transcranial magnetic stimulation (TMS) showed that both increased excitability of corticomotoneurons and reduced intracortical inhibition (ICI) contribute to motor cortex hyperexcitability. The aim of the study was to establish how different mechanisms interact to promote motor system hyperexcitability in amyotrophic lateral sclerosis (ALS) in relation to their clinical features.

Methods: The resting motor threshold (RMT), the motor evoked potential (MEP) recruitment curve and the cortical silent period (CSP) to single-pulse TMS were evaluated in 51 patients with ALS. Early ICI and intracortical facilitation (ICF) and late ICI were evaluated by paired TMS.

Results: The main abnormal TMS findings were: (a) a steeper MEP recruitment curve associated with a lowering of the RMT; (b) reduced or even absent early and late ICI; (c) reduced CSP lengthening with increasing TMS intensity; ICF was not affected. RMT increased and the MEP recruitment curve became less steep with longer disease duration, but they did not correlate with the motor symptoms at occurrence of PN, whereas in 2 symptoms followed a decline in sural SAP ≥ 20%.

Conclusions: The increased gain in MEP recruitment with a lowering of the RMT appears to be a primary event reflecting an increase in the strength of corticospinal projections. On the other hand, inhibitory functions linked to multiple neurotransmitter systems decline with disease progression. Both depletions have been considered as accounting for the impaired inhibition.

P2354

LACOSAMIDE IN PAINFUL DISTAL DIABETIC NEUROPATHY: RESULTS OF A MULTI-CENTER, PLACEBO-CONTROLLED US TRIAL
A. Shaibani1, P. Kenney1, J. Simpson1, S. Bongardt1
1Nerve and Muscle Center of Texas, Houston, TX, 2Schwarz Biosciences GmbH, Raleigh, NC, USA, 3Schwarz Biosciences GmbH, Monheim, Germany

Objective: Lacosamide is being investigated as an anticonvulsant with analgetic properties.

Background: Lacosamide (SPM 927, R-2-acetamido-N-benzyl-3-methoxypropionamide) is a functionalized amino acid that has shown efficacy in animal models for pain and epilepsy.

Design/methods: 469 patients were randomized (1:2:2:2) to placebo (n=66), 200 (n=141), 400 (n=125), or 600mg/day (n=137) lacosamide treatment arms. Subjects titrated to their assigned dose and then entered a 12-week maintenance phase in which no dose adjustments were allowed. Subjects rated their pain twice daily using an 11-point Likert scale. Adverse events (AEs) were assessed throughout the trial.

Results: Mean reduction in pain scores from baseline to the last 4 weeks of maintenance were approximately 1.67, 2.01, 2.29, and 2.23 under placebo, 200, 400, and 600 mg/day lacosamide, respectively, and approached significance (p=0.0507) for 400 mg/day lacosamide. A statistically significant separation between 400 and 600 mg/day lacosamide and placebo was achieved early during titration and continued for the entire titration and maintenance period. Most AEs were mild or moderate in intensity and started during the titration phase. The rate of early discontinuations was 31.8%, 32.6%, 43.2%, and 66.4% under placebo, 200, 400, and 600 mg/day lacosamide, respectively. The most frequently reported AEs were dizziness, nausea, balance disorder, tremor, and headache. Cognitive and behavioural AEs were relatively low, weight change and oedema were uncommon (<1%).

Conclusions: Lacosamide at doses of 400 mg/day and 600 mg/day significantly reduced pain scores in subjects during titration and the entire 12-week maintenance period of this trial.

P2355

THALIDOMIDE NEUROTOXICITY: IS IT REVERSIBLE? RESULTS OF A PROSPECTIVE LONG-TERM FOLLOW-UP STUDY
C. Brianı1, G. Zara1, R. Rondinone1, A. Doria2, L. Battistin1
1Department of Neurosciences, 2Department of Rheumatology, University of Padova, IRCCS San Camillo Hospital, Venice, Italy

Background: Sensory axonal neuropathy (PN) is a severe side effect of thalidomide therapy.

Aims: To evaluate the occurrence of PN in patients treated with thalidomide and to assess whether the PN, when occurs, is reversible.

Methods: 14 female patients, median age 35.5 years, treated with thalidomide for cutaneous lupus erythematosus were prospectively followed-up. Prior to, and regularly during treatment patients underwent neurological and electrophysiological evaluations. A decline in sural SAP ≥ 50% from baseline value was considered as criterion of sensory axonal PN.

Results: 10 patients (71.4%) developed PN. Only 6 complained of symptoms at occurrence of PN, whereas in 2 symptoms followed a few months after the electrophysiological evidence of PN. The median time free from PN complication was 15 months (95% C.I.: 12 – na). All 10 patients had an electrophysiological follow-up (median 24.2 months) after discontinuation of thalidomide. 5 presented electrophysiological improvement, which was complete in 4 (at 27.6, 36.5, and 38 months) and partial in 1 at 38 months. In the remaining 5 patients no electrophysiological changes were detected in 3, at 13.5, 21.5, and 12 months after stopping thalidomide. In 2 patients electrophysiological findings worsened even more after thalidomide discontinuation.

Conclusions: PN is a common complication of thalidomide therapy. In half of our patients PN improved after discontinuation of
the drug, and in 4 the recovery was complete. Our population was homogeneous as to disease and sex, and factors predictive of recovery could not be identified. A pharmacogenetic susceptibility may play a role.

P2356
REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN ALS: TIME FOR A THERAPEUTICAL TRIAL?
M. Dileone, F. Pilato, F. Ranieri, F. Capone, P. Proifice, G. Musumeci, D. Tagliente, F. Angelucci, M. Sabatelli, P.A. Tonali, V. Di Lazzaro
Department of Neurology, Catholic University of Rome, Italy

Introduction: Repetitive transcranial magnetic stimulation (rTMS) of the brain can modulate cortical neurotransmission. A novel paradigm of repetitive stimulation called continuous theta-burst stimulation (cTBS) produces a pronounced and lasting suppression of cortical excitability. The aim of this preliminary study was to investigate whether cTBS of the motor cortex could have any beneficial effect in patients with amyotrophic lateral sclerosis (ALS).

Methods: We performed a double-blind, placebo-controlled trial on 20 patients with a definite diagnosis of ALS. They were randomly allocated to active or placebo stimulation. Repetitive stimulation of the motor cortex was performed for 5 consecutive days every month for 6 consecutive months. The primary outcome was the rate of decline as evaluated with the ALS functional rating scale. The treatment was well tolerated by the patients. 15 patients (7 active and 8 sham) completed the study and were included in the 6-months analysis.

Results: Both active and sham patients deteriorated during treatment, however, active patients showed a modest but significant slowing of the deterioration rate. Though we cannot be sure whether the effects observed can be attributed to cTBS, because of the restricted number of patients studied, further investigation on a larger group of ALS patients is warranted.

Conclusion: The results of the pilot study might open up a new therapeutic perspective in ALS based on neuromodulation.

P2357
ELEVATED GLYCOSYLATED HEMOGLOBIN IS ASSOCIATED WITH SUBCLINICAL NEUROPATHY IN NEUROLOGICALLY ASYMPTOMATIC TYPE-2 DIABETIC PATIENTS: A PROSPECTIVE STUDY
K. El-Salem1, F. Ammari2, Y. Khader1, O. Dhaimat1
1Department of Neurosciences, 2Department of Medicine, Jordan University of Science and Technology, Irbid, Jordan

Background and aim of study: The association between poorly controlled diabetes and higher risk of peripheral neuropathy is well established. The American Diabetes Association (ADA) recommends that HbA1c should be less than 7%. Most previous studies used higher HbA1c cut points and focused only on symptomatic patients. This study aims to evaluate the association of elevated HbA1c using the 7% cut point, with subclinical neuropathy (asymptomatic patients) in type-2 diabetes (DM-II).

Methods: 50 consecutive asymptomatic diabetic patients with normal neurological exams were included. HbA1C was measured at the time of inclusion and three months later followed by nerve conduction studies (NCS). Average HbA1C 7% was considered elevated. Peroneal and median motor and sural and ulnar sensory nerves were tested. Univariate and multivariate analysis with logistic regression models were used to study the association of different patient characteristics in predicting abnormal NCS.

Results: 15 women and 35 men (age 51.6±10.8 years) were studied. Half of the patients had elevated HbA1c (mean: 8.7±2.1). The other half had HbA1c <7% (mean: 6.5%±1.5). Patients with elevated HbA1c were older and had longer disease duration (p<0.05). 26 patients (52%) had subclinical neuropathy (18 men, 8 women). In multivariate analysis, HbA1c was associated with higher risk of subclinical neuropathy (adjusted OR 10.71 (2.49, 46.01), p<0.005). When considering HbA1c as a continuous variable, each one-unit increase in HbA1c doubled the risk of subclinical neuropathy.

Conclusions: Subclinical neuropathy commonly exists in type-2 DM patients, and can be anticipated by elevated HbA1c.

P2358
PERIPHERAL NEUROPHYSIOLOGICAL CHANGES IN CYSTIC FIBROSIS PATIENTS: A PROSPECTIVE COHORT STUDY
K. El-Salem1, S. Aburahma1, M. Rawashdeh1
1Department of Neurosciences, 2Department of Paediatrics, Jordan University of Science and Technology, Irbid, Jordan

Aims: To study the frequency and pattern of peripheral neurophysiological changes in cystic fibrosis patients.

Methods: This is a prospective cohort study where consecutive cystic fibrosis patients older than two were recruited from the paediatric gastroenterology clinic over a period of 6 months. Patients with diabetes mellitus were excluded. 25 patients (14 males, 11 females) were included, with mean age of 11±5.6 years. All patients were neurologically asymptomatic. Nerve conduction studies were performed on the peroneal and median motor nerves, and median, ulnar and sural sensory nerves on one side. Distal and F-wave latencies, amplitudes and conduction velocities were studied for motor nerves. Latencies and amplitudes were studied for sensory nerves.

Results: 14 patients (56%) (9 males, 5 females), had neuropathy. All abnormalities were found in the sensory nerves. Ulnar sensory was abnormal in 48% of patients, sural sensory in 44%, and median sensory in 28%. Amplitudes were affected in all abnormal studies, whereas prolonged latencies were affected in 20% of sural responses, 8% of ulnar responses and 4% of median responses. Concordant abnormalities in the 3 nerves were found in 5 patients (20%). 5 patients had one upper and one lower extremity abnormal nerves. Presence of neuropathy was neither related to gender nor to age or disease duration. Motor nerves were not affected in any patient.

Conclusions: Cystic fibrosis can be associated with sensory peripheral nerve disease, with a predominantly axonal pattern. Peripheral nerve function should be followed up in these patients, clinically and neurophysiologically.

P2359
EVIDENCE FOR SYSTEMIC MICROINFLAMMATION IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS
D. Keizman1, O. Rogowski2, S. Berliner1, I. Artamonov1, G.B. Groozman1, N. Maimon4, D. Gross5, V.E. Drory1
1Department of Neurology, 2Department of Internal Medicine H, 3Department of Medicine D, 4Department of Oncology, 5Department of Respiratory Rehabilitation, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
**Background:** Amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular disease, the exact etiology of which is still unknown. Recent evidence suggests that neuro-inflammation may influence onset and/or progression of disease.

**Aim:** to determine the intensity of systemic inflammation in clinically asymptomatic (without overt infection and/or inflammation) ALS patients, in order to determine whether the existence of ALS itself is associated with a heightened inflammatory activity, and whether it has prognostic significance.

**Patients and methods:** The study group consisted of ALS patients from the ALS out-patient clinic at the Tel Aviv Medical Center. The control group was selected from the database of the Tel Aviv Medical Center Inflammation Survey. The following inflammatory parameters were compared between the groups: the erythrocyte sedimentation rate (ESR), fibrinogen and C-reactive protein concentrations, leukocytes count, and the neutrophils to lymphocytes ratio. Moreover, the correlation between inflammatory parameters and the disability status of the patients, as expressed by the ALS Functional Rating Scale (ALSFRS-R), was evaluated.

**Results:** 62 patients (21 women, 34%) were included. Their mean age was 58.7±13.9 years. For each patient we found a perfectly matched control from the database. CRP, fibrinogen and the neutrophils to lymphocytes ratio were significantly (p=0.001, 0.01, 0.01 respectively) elevated in the patients group. A statistically significant inverse correlation was found between ALSFRS-R and CRP, ESR, and fibrinogen levels (p=0.026, 0.034, <0.001 respectively).

**Conclusions:** Our findings suggest that ALS patients harbour a heightened systemic microinflammation that is possibly related to their pathogenesis, and is correlated to their disease stage.

**P2360**

**RECOMBINANT HUMAN ERYTHROPOIETIN SUPPRESSES SYMPTOM ONSET AND PROGRESSION OF G93A-SOD1 IN A MOUSE MODEL OF ALS BY PREVENTING MOTOR NEURON DEATH AND INFLAMMATION**

S.H. Koh1, G. Han1, H.Y. Kim1, K.Y. Lee1, Y.J. Lee1, H.T. Kim1, J.Kim1, B. Chung1, H.I. Yoo1, Y.B. Lee1, S.H. Kim1

1Department of Neurology, College of Medicine, Hanyang University, Seoul, 2Department of Neurology, Hanaum Hospital, Cheju, 3Department of Neurology, Bundang Jesaeng Hospital, Kyunggi Province, 4Department of Neurology, Gachon University, Inchon, South Korea

Multifactorial pathogenic mechanisms including inflammation, attenuated survival signals and enhanced death signals are involved in amyotrophic lateral sclerosis (ALS). Erythropoietin (EPO) has recently been highlighted as a cytokine with various potent neuroprotective effects including reduction of inflammation, enhancement of survival signals and prevention of neuronal cell death. This study was undertaken to evaluate the effect of recombinant human EPO (rhEPO) on ALS model mice. We treated 96 ALS model mice with vehicle only, or 1, 2.5 or 5iu of rhEPO per gram of mouse once per every other week after 60 days of age. The treatment significantly prolonged symptom onset and life span, preserved more motor neurons, enhanced survival signals, and attenuated inflammatory signals in a dose-dependent manner.

These data suggest that treatment with rhEPO represents a potential therapeutic strategy for ALS.

**P2361**

**ALTERNATIVE PARAMETER OF QUANTITATIVE SENSORY TESTING: THE DIFFERENCE BETWEEN HEAT PAIN AND WARM PERCEPTION THRESHOLDS IN PATIENTS WITH POLYNEUROPATHY AND HEALTHY INDIVIDUALS**

M. Nebuchennykh1, S. Loseth2, S.I. Mellgren2

1Department of Neurology, University Hospital of North Norway, 2Department of Neurology, Institute of Clinical Medicine, University of Tromsø, Norway

**Background and aims:** Elderly individuals and patients with polyneuropathy often perceive heat pain instead of or almost at the same time as warm perception when quantitative sensory testing (QST) is performed. We therefore compared the difference between heat pain and warm perception thresholds (DiffHP-WT) in order to explore whether this parameter is more strongly expressed in patients with peripheral neuropathy than in age and gender matched healthy individuals.

**Subjects and methods:** 36 patients (23 women, 13 men, 52.8 (12.2) (mean (SD)), (range 33–75 years) with symptoms and signs of polyneuropathy and 36 healthy persons (53.0 (12.3), range 34–74 years) matched according to age and gender were included. QST (using method of limits) was performed with SENSELab- THERMOTEST (Somedic, Sweden) recording warm, cold and heat pain perception thresholds on the distal calf and on the dorsal foot. DiffHP-WT in these locations was then calculated.

**Results:** DiffHP-WT in the lower calf was 3.4 (3.5) in the patients and 5.9 (3.6) centigrades in the controls (p=0.007), while on the foot it was 3.6 (2.9) versus 5.3 (3.8) centigrades (p=0.03). Only DiffHP-WT in the foot was significantly associated with age (in patients: r=0.63, p=0.0001; in healthy individuals: r=0.45, p=0.006).

**Conclusions:** QST with recordings of temperature perception and warm pain perception thresholds is a useful and sensitive method in evaluation of patients with small fibre polyneuropathy. We propose DiffHP-WT (difference between heat pain and warm perception thresholds) as an additional parameter reflecting the functional condition of unmyelinated C-fibres.

**P2362**

**RESPIRATORY INSUFFICIENCY AND NEURONAL LOSS IN THE MEDULLARY RETICULAR FORMATION IN MYOTONIC DYSTROPHY. A CLINICO-PATHOLOGICAL STUDY**

S. Ono, H. Mikami, T. Watanabe, T. Irie, T. Yamazaki, M. Suzuki

Department of Neurology, Teikyo University Chiba Medical Center, Ichihara, Chiba, Japan

**Objective:** To determine whether the medullary reticular formation is related to respiratory insufficiency in myotonic dystrophy (MyD).

**Background:** Respiratory insufficiency occurs frequently in patients with MyD. Recent data suggests that respiratory failure results from a primary dysfunction of the central nervous system in MyD. The autonomic respiratory centre is thought to be located in the medullary reticular formation. However, there have been few studies in MyD patients regarding possible relationships between lesions in the medullary reticular formation and the presence of alveolar hypventilation.

**Methods:** 7 patients with MyD and 8 age-matched controls were used. Alveolar hypoventilation of central type occurred in three MyD patients. We measured neurons in the dorsal central medullary nucleus (DCMN), the ventral central medullary nucleus (VCMN), and the subtrigeminal medullary nucleus (SMN).
Results: The densities of neurons of the DCMN and the VCMN in MyD patients with hypoventilation (4.07±0.47 mm² and 2.77±0.25 mm²) were significantly lower than in MyD without hypoventilation (5.73±0.54, p<0.01 and 4.42±0.97, p<0.05) and controls (5.78±0.77, p<0.01 and 4.48±0.95, p<0.02). The density of neurons of the SMN in MyD with hypoventilation (9.07±1.00 mm²) was significantly decreased (p<0.01 and p<0.001) versus MyD without hypoventilation (15.1±1.15) and controls (17.3±1.31).

Conclusion: These data suggest that the neuronal loss of the DCMN, the VCMN, and the SMN is associated with the presence of respiratory insufficiency in MyD.

P2363
ASSOCIATION OF ULTRASOUND AND EMG IN A NEUROPHYSIOLOGICAL LAB CONTRIBUTED TO IMPROVE DIAGNOSTIC SENSITIVITY AND THERAPEUTICAL DECISION IN FOCAL NERVE IMPAIRMENT: ONE YEAR OF SYSTEMATIC ASSESSMENT
L. Padua1,2, I. Aprile1,2, C. Pazzaglia1,2, G. Frasca1, P. Caliandro1,2, P. Tonali1,2, C. Martinoli1
1Institute of Neurology, Università Cattolica del Sacro Cuore, Fondazione Don Carlo Gnecchi, Roma, 2Cattedra di Radiologia R-DICM, Università di Genova, Italy

Objective: To evaluate the usefulness of the combination of electromyography evaluation (EMG) and ultrasound (US) assessments in the diagnosis of nerve trunk involvement. We hypothesised that in some cases, which are clinically or neurophysiologically unclear, the simultaneous study of the peripheral nervous system through ultrasound and EMG could provide etiopathologic information, achievable not only through EMG, and sometimes it would have been able to modify a therapeutic decision.

Methods: During 2005, we performed a prospective study in 77 consecutive patients with an involvement of a single nerve trunk through a combination of EMG and ultrasound in the same session. We divided diagnostic contribution of ultrasound into 4 groups: diagnostic, confirming, inconclusive and misdiagnostic.

Results: In about a quarter of patients ultrasound provided results confirming clinical-neurophysiological diagnosis. In another quarter of cases, ultrasound was very helpful to modify the diagnosis and therapy: in most cases the contribution of ultrasound is important to detect tumours or cysts showing, in this manner, the cause of nerve involvement. In half of the cases, ultrasound appeared inconclusive and in one case it was misdiagnosed.

Conclusions: The combination of EMG and ultrasound performed in the same session (or in a synergic collaboration with ultrasound examiner) may be very useful thanks to a feedback mechanism in the same session (or in a synergic collaboration with ultrasound.)

P2365
SERUM LEVELS OF THE FIBROBLAST GROWTH FACTOR AND INSULIN-LIKE GROWTH FACTOR IN AMYOTROPHIC LATERAL SCLEROSIS PATIENTS
P. Bongioanni1, M.R. Metelli1, F. Fulceri2, F. Manzone3, B. Rossi4, P. Pietrini5
1Department of Neuroscience, 2Department of Experimental Pathology, University of Pisa, Italy

Background: Fibroblast Growth Factor (bFGF) and Insulin-like Growth Factor (IGF-1) are trophic factors for motor neurons and glial cells. In such neurodegenerative diseases as Amyotrophic Lateral Sclerosis (ALS), there is an imbalance between neurotrophic and neurotoxic factors.

Methods: We assayed repeatedly over a two-year period bFGF and IGF-1 in sera from 49 ALS patients. Disease severity was scored by means of the ALS Functional Rating Scale, and patients subgrouped accordingly into 3 classes: I, II, and III. Growth factors were quantified by enzyme-linked immunosorbent assay (ELISA).

Results: Growth factors data concern assays at time of diagnosis (T0) and those at time of the most recent clinical examination (Tn). Mean bFGF levels were lower, in both class I and class II patients, at Tn vs. T0 and significantly in class I vs. class II at Tn vs. T0. Mean bFGF levels were higher in class II vs. class III patients at Tn vs. To. Mean sIGF-1 levels were significantly higher, in both class I and class II patients, at Tn vs. T0. Mean sIGF-1 levels were higher in class I vs. class II and class II vs. class III patients at Tn vs. T0.

Conclusion: Although changes over time of serum bFGF are not univocal, neither related to disease progression nor to disease severity, IGF-1 values in sera from ALS patients seem to be directly linked to a biological response against neurotoxic noxae, as if a milder disease state is maintained for a longer period of time it is related to enhanced IGF-1 production.

P2366
PRIMARY CO-ENZYME Q10 DEFICIENCY IN AN ADULT
J. Schaefer1, M. Weinhold1, P. Navas2, K. Geiger3, H. Reichmann1, S. Jackson3
1Department of Neurology, University of Dresden, Dresden, Germany, 2Division of Cellular Biology, Universidad Pablo de Olavide, Sevilla, Spain, 3Division of Neuropathology, University of Dresden, Germany
Background: Intracellular lipid accumulations are a striking feature of several metabolic myopathies, in particular defects of mitochondrial fatty acid oxidation and of the respiratory chain. Despite new diagnostic methods like tandem mass spectrometry and molecular genetic analyses, many patients still pose considerable diagnostic and therapeutic problems.

Case report and methods: A male patient developed in his 2nd decade slowly progressive proximal muscle weakness associated with permanent myalgias, which occurred both at rest and during muscular exertion. After 20 years into the disease the patient’s maximal walking distance was only 100 m, and he required opiates for his meanwhile unbearable myalgias. Lactate concentrations were markedly elevated in blood and brain tissue (MR spectroscopy). Plasma acylcarnitine analysis revealed elevated levels of fatty acid intermediates of all chain lengths. A muscle biopsy showed a severe lipid storage myopathy.

Results: The enzyme activities of respiratory chain complexes I-IV were normal, but the combined activities of Cx I-III and Cx II-III were reduced suggesting a coenzyme Q10 deficiency. Coenzyme Q10 concentrations were greatly reduced in fibroblasts thus proving the diagnosis of primary coenzyme Q10 deficiency. Under a therapy with riboflavin and CoQ10 the patient’s condition stabilized initially, but when the patient ceased to take coenzyme Q10 he deteriorated again.

Conclusions: Primary coenzyme Q10 deficiency should always be considered as a differential diagnosis of lipid storage myopathy, because it is one of the few metabolic disorders for which an effective therapy has been established.

P2367

COMPARING THE SAFETY AND TOLERABILITY OF DULOXETINE FOR THE MANAGEMENT OF DIABETIC PERIPHERAL NEUROPATHIC PAIN BETWEEN PATIENTS WITH AND WITHOUT HISTORICAL AND/OR CO-MORBID CARDIOVASCULAR CONDITIONS

J. Wernicke, A. Prakash, D. Kajdasz, J. Houston Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA

Background: We compared the safety of duloxetine between patients with and without historical (Hx) or co-morbid CV conditions at baseline.

Methods: Data were pooled from 3 double-blind studies in adult patients with DPNP. Patients were randomized to duloxetine (DLX) 60 mg OD (N=339), 60 mg BID (N=341), or placebo (PBO) (N=339) for 12 weeks. Safety assessments included discontinuations, treatment-emergent adverse events (TEAEs) and BP changes.

Results: Mean age of patients with Hx/co-morbid CV conditions (n=762) was 61.1 yrs and in patients without Hx/co-morbid CV conditions (n=262) was 56.1 yrs. Common Hx/co-morbid CV conditions were hypertension (65%), coronary artery disease, and myocardial infarction. Diabetes medications, antihypertensives, cholesterol-lowering agents, analgesics, and levodopa were the most commonly used concomitant medications. Discontinuation due to AEs were higher for DLX vs. PBO in both subgroups (13.5% DLX, 6.0% PBO and 14.3% DLX, 3.4% PBO respectively) in patients with and without Hx/co-morbid CV conditions. CV-related TEAE rates in patients with (8.4% DLX; 9.9% PBO) and without (8.6% DLX; 6.0% PBO) Hx/co-morbid CV conditions were similar (p=0.1 for tx by subgroup interaction). The effect of DLX vs. PBO on mean changes in SBP and DBP between patients with and without Hx/co-morbid CV conditions was not statistically significant (p>0.1 for tx by subgroup interaction). Sustained hypertension rates were similar between patients with (2.4% DLX; 2.8% PBO) and without (2.9% DLX; 4.7% PBO) Hx/co-morbid CV conditions (p>0.1 for tx by subgroup interactions).

Conclusions: In this analysis, the safety of duloxetine in patients with DPNP was not significantly different between patients with and without Hx/co-morbid CV conditions.

P2368

GPX1 C953T POLYMORPHISM AND THE RISK OF SPORADIC ALS

Department of Neurology, Jagiellonian University, Departments of Neurology and Biochemistry, Medical University, Warsaw, Poland

Background and aims: Overproduction of hydrogen peroxide seems to be an important factor in the pathogenesis of amyotrophic lateral sclerosis (ALS). Glutathione peroxidase 1 (GPX1) is a key enzyme of the antioxidant defence system, which detoxifies hydrogen and lipid peroxides. The GPX1 gene is located on chromosome 3p21.3. The C953T functional polymorphism in exon 2 (rs1050450) results in substitution of leucine for proline at codon 198. The T-allele is associated with a decreased enzyme activity and decreased enzyme responsiveness to stimulation with selenium. We have studied for the first time the significance of the GPX1 gene 198Pro/Leu polymorphism in sporadic ALS (sALS) patients and in healthy controls.

Methods: We included 296 patients with a definite or probable diagnosis of sALS (El Escorial Criteria) and 469 healthy controls of similar age and gender. The GPX1 198Pro/Leu polymorphism was detected by PCR amplification and restriction enzyme digestion.

Results: The distribution of the studied GPX1 198Pro/Leu polymorphism was in Hardy-Weinberg equilibrium among both the cases and the controls (p>0.05). The genotype distribution of the GPX1 gene was similar in patients with sALS and in their respective controls. Patients with sALS: Pro/Pro: 137 (46.3%), Pro/Leu: 136 (45.9%), Leu/Leu: 23 (7.8%) vs. controls: Pro/Pro: 218 (46.5%), Pro/Leu: 205 (43.7%), Leu/Leu: 46 (9.8%); p=n.s. No correlations were found between the studied polymorphism and the age of disease onset, and clinical type of ALS (bulbar vs. limb onset).

Conclusions: The GPX1 gene 198Pro/Leu polymorphism was not associated with the risk of sALS in a cohort of Polish patients.

P2369

VASCULAR ENDOTHELIAL GROWTH FACTOR GENE POLYMORPHISMS AS A RISK FACTOR IN SPORADIC AMYOTROPHIC LATERAL SCLEROSIS IN A POLISH POPULATION
B. Tomik, A. Słowiński, A. Gienia, D. Zawislak, M. Ostrowska, A. Szczudlik

Department of Neurology, Jagiellonian University, Krakow, Poland

Background: Genetic factors involved in the pathogenesis of sporadic amyotrophic lateral sclerosis (sALS) still remain largely unknown. One candidate gene might be the vascular endothelial growth factor (VEGF), which is a major factor for normal and pathological angiogenesis, but it also directly affects the neuronal cells and regulates neuronal blood flow. Recent studies showed that -634 G/C and -2578 C/A polymorphisms of the VEGF gene were associated with a greater risk of sALS.

Objective: We have studied a possible association between -634 G/C and -2578 C/A polymorphisms of the VEGF gene and the risk factor of sALS in the Polish population.

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
Material and methods: We included 204 unrelated patients with sALS and 348 unrelated healthy controls matched for age and sex. The definite or probable diagnosis of ALS was established according to El Escorial Criteria (1998) in Krakow MND Center. The polymorphisms were studied by polymerase chain reaction (PCR) and restricted enzyme digestion.

Results: VEGF -634 and VEGF -2578 genotype frequency in patients with sALS (GG-0.57, GC-0.36, CC-0.07; CC-0.22, CA-0.51, AA-0.27) and controls (GG-0.53, GC-0.38, CC-0.09; CC-0.23, CA-0.52, AA-0.25) were very similar and did not influence the risk of occurrence of sALS (p=0.5704; p=0.8106).

Conclusion: Although some previous studies discovered an association with polymorphisms' VEGF gene and risk of sALS in a few European populations, we demonstrated that -634 G/C and -2578 C/A polymorphisms of the VEGF gene are not connected with the greater risk of sALS in the Polish population, which was also shown in German, Dutch and London populations.

P2370
HIGH-RESOLUTION ULTRASOUND AS AN ADJUNCTIVE DIAGNOSTIC TECHNIQUE IN COMMON PERONEAL NEUROPATHY
M.T. Ahmad, Y.L. Lo
Department of Neurology, NNI/SGH, Singapore, Singapore

Background: Electrophysiological localization of peroneal neuropathy can be technically challenging. Focal conduction block at the fibula head is often absent, and severe axonal degeneration renders interpretation of nerve conduction studies (NCS) difficult. Electromyography (EMG) may not give a precise location of abnormality, rendering exclusion of low sciatic nerve lesions uncertain. Ultrasound (US) may be of value in the anatomical visualization in this context.

Methods: We performed transverse view US measurements of the common peroneal nerve at the fibula head in 14 healthy controls. Studies were obtained with a SonoSite 5–10 MHz real-time linear array transducer.

Results: In healthy controls (8 men; age: 22 to 53), mean (standard deviation (SD)) of transverse diameter and cross-sectional area were 0.43 (0.08) cm and 0.9 (0.03) cm² respectively. The upper limits of normality at 2SDs were 0.6 cm and 0.16 cm². A 56-year-old female had bilateral foot drop of 18-months duration after operation on both knees. NCS showed markedly reduced right peroneal nerve conduction velocities, absent left peroneal motor responses. EMG suggested longstanding peroneal neuropathy at the fibula head region. Peroneal US showed bilateral significantly increased diameter and area (right: 0.78 cm, 0.28 cm²; left: 0.81 cm, 0.23 cm²).

Conclusions: Focal increase in diameter and area of the common peroneal nerve can be visualized with high-resolution US. This method is of potential value as a diagnostic adjunct in the localization of peroneal entrapment neuropathy in the lower limb.

P2371
AUTOIMMUNE DISEASE AND MYASTHENIA GRAVIS: ASSOCIATION WITH ACETYLCHOLINE RECEPTOR AND ANTI-MU-SK ANTIBODIES
E. Albertini¹, D.M. Bonifati², V. Romeo¹, A. Palmieri¹, E. Pegoraro¹, C. Angelini¹
¹Neuromuscular Center; Department of Neurosciences, University of Padova, Padova, ²Unit of Neurology, Department of Internal Medicine, S. Chiara Hospital, Trento, Italy

Background: Myasthenia gravis (MG) is an autoimmune disorder characterised by fluctuant weakness that affects mostly young women. MG can be associated with the presence of acetylcholine receptor antibodies (AChRab) in about 70-90% of patients and anti-MuSK antibodies in 10-50% of patients.

Objective: To evaluate the prevalence of other immune-mediated diseases in MG patients and the morbidity of auto-immune disease with auto-antibodies positivity.

Materials and methods: A retrospective evaluation of MG patients was performed: 207 MG patients (131 females and 76 males) were grouped into “seropositive” (SPMG) and “seronegative” (SNMG). Clinical features were evaluated through MGFA score. The presence of other immuno-mediated disorders within both groups was documented.

Results: We identified 157 SPMG (76%) and 45 SNMG. We considered separately anti-MuSK patients (5). The females were 63% among SPMG, 62% among SNMG and 4 among MuSK-positive. In 41 SPMG patients (26%) other immune-mediated diseases was identified. In particular we found an association with thyroid diseases in 21 patients (51%), diabetes in 7 patients, skin diseases in 7 patients. In 7 SNMG patients, only 15%, the presence of other immuno-mediated diseases was diagnosed; in particular we found thyroid diseases in 4 patients and 2 had skin disease. Among MuSK positive in 2 patient’s (40%) we found an association with immuno-mediated disease.

Conclusions: The present study demonstrates, that the occurrence of coexistence of autoimmune diseases in SPMG is more prevalent than in SNMG; which is more relevant for thyroid and skin diseases and diabetes. Surveillance of such comorbidity is strongly recommended.

P2372
O’SULLIVAN-MCLEOD SYNDROME. CLINICAL AND MAGNETIC RESONANCE IMAGING PRESENTATION: A CASE REPORT
K. F. Amthor¹, T. Pedersen²
¹Department of Neurology, Buskerud County Hospital, ²Department of Neuroradiology, Buskerud County Hospital, Drammen, Norway

Background: O’Sullivan-McLeod syndrome is a rare form of slowly progressive spinal muscular atrophy of the hands, first described in 1977. Only a few MRI studies regarding this condition have been published. In one series of 4 patients segmental atrophy of the spinal cord between C5 and T1 is described. In another case study MRI reveals symmetrical T2 weighted lesions in the region of the anterior horn cells from levels C2 to C7 with a normal spinal cord diameter.

Case report: The patient is a 22 year old healthy female without a family history of neurological disease. Since the age of 17 she slowly developed progressive bilateral wasting and weakness of the small hand muscles. Her proximal muscles and lower extremities were not affected. Neurological examination revealed marked atrophy and paresis of ulnar and median nerve innervated muscles with otherwise normal neurological findings. Motor and sensory nerve conduction velocities were normal. F-waves were delayed in the left ulnar nerve, and unmesurable in the right. There were no conduction blocks. Needle electromyography revealed a chronic neurogenic pattern within the intrinsic muscles of both hands. MRI of the cervical spine exposed marked atrophy from C4 to T2 with symmetrical T2 weighted high signals in the region of the anterior horn cells extending from C2 to T2.

Conclusion: According to our knowledge, this is the first case of O’Sullivan-McLeod syndrome reported with both spinal cord atrophy and symmetrical lesions in the region of the anterior horn cells demonstrated on MRI.
The study was funded by Pfizer, Inc.

**Conclusions:** Placebo-patients (fixed-dose [p<0.0001] or fixed-dose [p<0.0001]) were more likely to experience pain relief than placebo-patients. Week 1 treatment differences from placebo in change in mean allodynia VAS score: flexible-dosage, -10.0; fixed-dosage, -7.3. Corresponding endpoint values: -13.5; -7.2. Most common AEs: dizziness (flexible-dosage, 24%; fixed-dosage, 31%; placebo, 7%) and somnolence (11%, 19%, 2%). All-cause discontinuations: flexible-dosage, 5.5%; fixed-dosage, 20.5%; placebo, 16.7%.

**Conclusions:** Pregabalin-treated patients, 300 mg/d fixed-dosage or flexible-dosage, had rapid onset of clinically meaningful and sustained pain relief.

**Introduction:** Pregabalin has demonstrated efficacy in treating pain associated with fibromyalgia. This study further investigated efficacy and safety of pregabalin in fibromyalgia.

**Methods:** Randomized, double-blind, placebo-controlled with 1-week single-blind placebo run-in. Patients meeting ACR fibromyalgia criteria with pain VAS score ≥40 mm (0–100 mm scale), mean pain score ≥4 at randomization, and ≥230% reduction in pain VAS score during placebo run-in were randomized to pregabalin 300, 450, or 600 mg/d (BID) or placebo for 14 weeks (2-week dosage escalation; 12-week fixed-dosage). Primary efficacy parameter was endpoint mean pain score (MPS). Additional parameters included Patient Global Impression of Change (PGIC) and Medical Outcomes Study-Sleep (MOS) Problem Index.

**Results:** 745 randomized patients: 95% female, mean age=50 years, median fibromyalgia duration=10 years, baseline MPS=6.7. Differences from placebo in mean change from baseline to endpoint in MPS were: 300 mg/d, -0.71 (p=0.0009); 450 mg/d, -0.98 (p<0.0001); 600 mg/d, -1.00 (p=0.0001). Significantly greater proportions of patients reported at least minimal improvement on the PGIC with pregabalin: 68% of 300 mg/d, 78% of 450, 66% of 600 vs. 48% of placebo. Pregabalin doses at 300, 450 and 600 mg/d (p<0.0134, 0.0012, and p<0.0001, respectively) were associated with significant improvements in Overall MOS Sleep Problem Index. Most common AEs: dizziness (all pregabalin, 35.8% vs. placebo, 7.6%); somnolence (18.0% vs. 3.8%). Incidence of AEs associated with significant improvements in Overall MOS Sleep Problem Index. Most common AEs: dizziness (all pregabalin, 35.8% vs. placebo, 7.6%); somnolence (18.0% vs. 3.8%). Incidence of AEs appeared to increase with dosage.

**Conclusions:** Pregabalin demonstrated efficacy in pain relief, management of fibromyalgia and improved sleep outcomes. The study was funded by Pfizer, Inc.

**Background and aims:** To evaluate time to onset of clinically meaningful pain relief in PHN patients treated with pregabalin.

**Methods:** Eligible patients with PHN ≥3 months, pain VAS score ≥40 mm, and ≥24 daily pain scores during the 7-day screening period (average daily score ≥4; 0-10 scale). 91 randomized to flexible-dosage pregabalin (optimized for efficacy/tolerability to 150, 300, or 600 mg/d, BID); 88 to 300 mg/d fixed-dosage pregabalin; 90 to placebo for 4 weeks of treatment. Primary efficacy parameter was time to onset of clinically meaningful pain relief (≥1-point improvement in daily pain score plus decrease of ≥30% in weekly pain score at endpoint), summarized with Kaplan-Meier plots and tested for treatment differences using a Cox hazards model. Secondary measures included change in mean VAS score (100 mm scale) for brush-evoked allodynia in affected areas.

**Results:** Mean PHN duration=2.5 years; baseline mean pain score=6.3-6.7. Median time to meaningful pain relief: flexible-dosage, 3.5 days (P<0.0001); fixed-dosage, 1.5 days (P=0.0001); placebo patients, median time to meaningful pain relief exceeded study observation period, with <50% achieving ≥30% improvement. Pregabalin-treated patients (flexible-dose [p<0.0001] or fixed-dose [p<0.0001]) were more likely to experience pain relief than placebo-patients. Week 1 treatment differences from placebo in change in mean allodynia VAS score: flexible-dosage, -10.0; fixed-dosage, -7.3. Corresponding endpoint values: -13.5; -7.2. Most common AEs: dizziness (flexible-dosage, 24%; fixed-dosage, 31%; placebo, 7%) and somnolence (11%, 19%, 2%). All-cause discontinuations: flexible-dosage, 5.5%; fixed-dosage, 20.5%; placebo, 16.7%.

**Conclusions:** Pregabalin-treated patients, 300 mg/d fixed-dosage or flexible-dosage, had rapid onset of clinically meaningful and sustained pain relief.

**Background and aims:** To evaluate time to onset of clinically meaningful pain relief in PHN patients treated with pregabalin.

**Methods:** Eligible patients with PHN ≥3 months, pain VAS score ≥40 mm, and ≥24 daily pain scores during the 7-day screening period (average daily score ≥4; 0-10 scale). 91 randomized to flexible-dosage pregabalin (optimized for efficacy/tolerability to 150, 300, or 600 mg/d, BID); 88 to 300 mg/d fixed-dosage pregabalin; 90 to
P2376
AMYTOTRAPHIC LATERAL SCLEROSIS AND TRANSCALLOSAL INHIBITION
L.F. Bolokadze, I.F. Fedotova
Department of Neurology, Academy of Medical Science, Kharkov, Ukraine

Objective: Assessment of upper motor neuron (UMN) involvement is essential for the diagnosis of amyotrophic lateral sclerosis (ALS). In a number of ALS cases, mirror movements (MM) suggest an involvement of transcallosal fibre tracts in conjunction with UMN involvement. The present study analysed whether deficient transcallosal inhibition (TI) tested by TMS enables detection of cortical affection in ALS, even at early stages of the disease.

Methods: In 7 patients with definite ALS and 19 patients with early ALS (aged 67.5+/6.7 years) TMS investigation included analysis of contralateral (cMEP) and ipsilateral (iMEP) motor evoked potentials as well as measurement of TI (latency, duration) with recording from both first dorsal interosseus muscles.

Results: Clinical UMN signs were present in 6 patients. 87.4% of patients showed a pathological TI (prolongation or loss of TI). 5 of 8 ALS patients showing a pathological TI had no clinical UMN signs. 2 of these patients showed MM. One patient displayed also pathological findings in TI investigation.

Conclusions: Our findings suggest a functional deficit of transcallosal fibre tracts even at early stages of the disease still lacking clinical UMN signs. Measurement of TI tested by TMS can detect an involvement of the cortical output system in ALS and may be helpful in an early assessment of the diagnosis.

P2377
HOW IS OCCUPATION ASSOCIATED WITH THE OCCURRENCE OF CARPAL TUNNEL SYNDROME
M. Bucuk, D. Bonifacic, A. Jurjevic, Z. Tomic, L. Tuskan-Mohar
Department of Neurology, Clinical Hospital Rijeka, Croatia

Objective: The present study seeks to determine the association of occupation in patients with carpal tunnel syndrome.

Background: Carpal tunnel syndrome (CTS) is caused through the compression of the median nerve in the carpal tunnel.

Patients and methods: We analyzed age, sex and occupation of patients who were diagnosed with CTS. This was done via physical examination and electromyographic analysis in Electromyography laboratory in the Department of Neurology of Clinical Hospital Rijeka in 2006. Patients whose median nerve was destroyed as a result of trauma, diabetes mellitus, rheumatoid arthritis or some other illness were not included in our study.

Results: We analyzed occupation, age and sex of 273 patients who were diagnosed with CTS. Carpal tunnel syndrome is more than twice as common in women as it is in men. Patients who are over 55 are more likely to suffer from CTS. Women with CTS were more likely exposed to moderate manual work. While men with CTS were more likely to have worked in stressful office/clerical jobs.

Conclusions: Carpal tunnel syndrome is more than twice as common in women as it is in men. Patients over 55 are more likely to suffer from CTS. Women with CTS are more likely having been exposed to moderate manual work, while men with CTS were more likely to have worked in stressful office/clerical jobs.

P2378
AUTOIMMUNE NECROTIZING MYOPATHY AND ANTI-JO1 ANTIBODIES: A CASE OF STEROID RESPONSIVE INFLAMMATORY MYOPATHY
D.M. Bonifati1, G. Paolazzi2, M. Fanin1, C. Angelini1, D. Orrico1
1Unit of Neurology, Santa Chiara Hospital, 2Department of Internal Medicine, Santa Chiara Hospital, Trento, 3Unit of Neuropatologia, Neurosciences Department, University of Padova, Italy

Background: Between idiopathic inflammatory myopathies (IIM), autoimmune necrotizing myopathy seems to have peculiar clinical and histopathological features but few cases are described in the literature.

Case report: A 42-year-old woman noted slowly progressive weakness over 4 months. The weakness was mainly proximal in the lower limbs with difficulties in swimming and climbing stairs. Motor milestones were normal and no family history for neuromuscular disease was present. Due to the progressive course of the disease the patient was admitted to a district hospital where CK was found elevated (above 30 times) and a muscle biopsy showed widespread necrotic, and regenerating muscle fibres. Phagocytes were present only around necrotic fibres. A primitive dystrophic myopathy was supposed. After a couple of months we saw the patient when also upper limb proximal muscles were affected and Gowers manoeuvre was possible only with an object. Considering the subacute course of the disease, an immunological screening was performed and a trial with prednisone 50 mg daily was started. We found positive anti-Jo1 antibodies and an elevated CD4/CD8 ratio. On prednisone muscle strength rapidly improved and CK decreased until both normalised in 2 months. A thorough screening for malignancies, including total body PET, was negative.

Conclusion: Autoimmune necrotizing myopathy is probably a non-recognized form of IIM. In comparison with the few cases described in the literature, our patient was positive for anti-Jo1 antibodies and no cancer was found. A good and complete response to steroids is confirmed underlying the importance of a correct diagnosis.

P2379
PROTEOLYTIC ENZYMES, INVOLVED IN NEURONAL CELL DEATH, IN THE CEREBROSPINAL FLUID OF PATIENTS WITH AMYTOTRAPHIC LATERAL SCLEROSIS
L.V. Brylev1, A.A. Yakovlev1, M.V. Onufriev1, N.V. Gulyaeva1, M.N. Zakharova1
1Institute of Neurology RAMS, 2Institute of Higher Nervous Activity and Neurophysiology RAS, Moscow, Russia

The object for study was measurement of calpain, caspase-3 and cathepsin B activity in the cerebrospinal fluid (CSF) of patients with amyotrophic lateral sclerosis (ALS) and search for regulators of these enzymes in CSF. The study included 47 patients with ALS and 27 control subjects. We measured activity of calpain, caspase-3 and cathepsin B in CSF by fluorimetric assays based on the specific hydrolysis of Ac-LY-AMC, Ac-DEVD-AMC, Z-RR-AMC respectively. Calpain-like basic and acidic activities were detected in buffers pH 7.4 and pH 5.5 respectively. The regulation of pure enzymes activity by CSF was evaluated by the same assay but in presence of purified human calpain I, recombinant human caspase-3, purified bovine cathepsin B. LDH activity was also detected. Calpain-like acidic activity was increased in CSF of patients with ALS. This activity was blocked in presence of calpain inhibitor ALLN in concentration-dependent manner. The activity of LDH was increased in CSF of patients with ALS and signific-

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
anty correlated with calpain-like activity. The activities of caspase-3 and cathepsin B were under detection limit. CSF from both groups activated recombinant caspase-3, inhibited purified calpain I and cathepsin B. The inhibition of calpain I was significantly increased in ALS patients. LDH activity correlated with the level of cathepsin B inhibition and there was a tendency toward correlation of LDH activity with the level of calpain I inhibition. Our results may demonstrate that accumulation of calpain-like protease and calpain inhibitor occur during cell death in the central nervous system of patients with ALS.

P2380
THORACIC OUTLET SYNDROME OR MULTIFOCAL MOTOR NEUROPATHY?
Department of Neurology, Clinical Hospital Centre Rijeka, University of Rijeka, Croatia

Objective: To present a case of a 21-year-old male with progressive weakness of the right hand and a diagnosis of thoracic outlet syndrome (TOS), our doubts about diagnosis and our consideration of multifocal motor neuropathy.

Methods: History data, physical examination, radiography of cervical spine and chest, cervical spine MR, helical computed tomography (CT) angiography, needle electromyography (EMG) and nerve conduction studies were performed.

Results: The atrophy of the right thenar was the first symptom leading to diagnosis of carpal tunnel syndrome. Later on weakness spread to hypothenar, intrinsic muscles and wrist flexors with mild paresthesias. Provocative tests were interpreted as positive and TOS was diagnosed. Blood, urine and cerebrospinal analyses were normal. Radiography of cervical spine showed massive C7 transverse processes, particularly on the right side. The cervical spine MR as well as the helical CT angiography were done and did not show any compression of the lower trunk of the brachial plexus or the subclavian artery. Electromyographic studies of hand and forearm muscles revealed reduced innervation pattern indicating a chronic neurogenic lesion as seen in motor neuron disease (MND). Nerve conduction studies excluded MND or TOS demonstrating multifocal motor neuropathy with conduction block.

Conclusion: The patient’s symptoms, physical examination, provocative tests and radiography, at the beginning pointed to TOS. However, it was excluded with additional diagnostic procedures and the results of nerve conduction studies leading to diagnosis of MNM.

P2381
LEVETIRACETAM EFFECTIVENESS IN HEMIFACIAL SPASM
P.B. Carriover, M. Petracca, S. Montella
Department of Neurological Sciences, University of Naples Federico II, Napoli, Italy

Background: Hemifacial spasm (HFS) consists of unilateral involuntary contractions of facial muscles, innervated by the seventh cranial nerve. Although HFS is a benign condition, it can cause significant cosmetic and functional disability. Levetiracetam indication concerns the treatment of partial seizures with or without secondary generalization in epilepsy, but anecdotal reports indicate his effectiveness in the treatment of tardive dyskinesia. We report a patient with HFS who responded favourably to levetiracetam.

Method: In June 2006 we examined a man aged 54 years with a 5-year history of left-sided HFS, characterized by involuntary tonic-clonic contractions of eye and mouth orbicular muscles and platysma and involuntary eye closure interfered with vision. Biochemical analysis of blood and MR angiography of the cerebellopontine angle were normal. The patient was treated with levetiracetam (500 mg/day increased after 5 days at 500 mg x 2/day).

Results: After 3 weeks of treatment, there was a significant regression of symptoms and visible spasm. Botulinum toxin type A infiltrations were given after 2 months in order to remove residual symptoms and levetiracetam was administered as adjunctive therapy. After 7 months of therapy with levetiracetam, the patient remained symptom-free with no adverse drug reactions.

Conclusion: Levetiracetam can be used as adjunctive therapy in HFS in association with botulinum toxin type A infiltrations and this could be a possible option for patients intolerant to botulinum infiltrations and an interesting alternative to repeated botulinum injections.

P2382
POLIOMYELITIS-LIKE SYNDROME IN A CASE OF NEUROBORRELIOSIS WITH CLINICAL-RADIOLOGICAL COHERENCE
V. Charles1, T.J. Duprez2, B. Kabamba3, A. Ivanou1, C.J. Sindic1
1Department of Neurology, Catholic University of Louvain, Louvain, 2Department of Radiology and Neuroimaging, Catholic University of Louvain, 3Department of Microbiology, Catholic University of Louvain, Cliniques Universitaires Saint-Luc, Brussels, Belgium

Background: Neuroborreliosis may occur as a painful meningoradiculitis in the early dissemination phase of Lyme disease, and as chronic encephalomyelitis in the late chronic phase. However, rare clinical variants have been reported, such as early incomplete transverse myelitis.

Case report: We present the clinical data of a 21-year-old man developing within two weeks a poliomyelitis-like syndrome characterized by a painless weakness in the proximal muscles of both arms. Diffuse fasciculations were noted without sensory deficits. Deep tendon reflexes were abolished in the right arm. Meningeal signs and symptoms were absent. Serum and CSF analysis revealed a high IgG and IgM antibody activity against Borrelia burgdorferi, with intrathecal antibody synthesis. A lymphocytic meningitis was also present. Spinal cord MR examination demonstrated abnormal T2 hypersignal intensity within the anterior horns of the central grey matter, and abnormal root-blood barrier breakdown on contrast-enhanced T1-weighted images, from C2 to Th1. A complete recovery was observed after antimicrobial treatment.

Conclusion: A radiculo-myelitis involving only the peripheral motor system at a motoneuronal and radicular level may be due to B. burgdorferi infection in the early dissemination phase of the disease process.

P2383
THYMIC ABNORMALITIES IN MYASTHENIA GRAVIS
O.C. Chebut, R.I. Balasa, E. Moldovan, M. Dan
Department of Neurology, Mures County Emergency Clinical Hospital, Targu-Mures, Romania

Introduction: Myasthenia gravis (MG) is an autoimmune syndrome caused by the failure of neuromuscular transmission, which results from the binding of autoantibodies to proteins involved in signalling at the neuromuscular junction (NMJ).

Material and method: We have reviewed clinical and imagistic features, muscular tissue biopsy, thymus histology and outcome in
112 patients who underwent thymectomy between 1995–2006 in Murell County Emergency Clinical Hospital. The follow-up period ranged from 1 to 12 years, mean 6.3 years.

**Results:** Sex: 69 women; age: between 19 and 63, mean 33.5 years; clinical: ocular MG – 18%, mild generalized – 56%, moderately severe generalized – 16%, acute fulminating – 1%, late severe – 9%; association with other autoimmune diseases: 12% cases; – imagistic/CT of the thorax: single hyperdense mass, well delimited – 56.25%, multiple hyperdense nodules – 31.25%, hypodense mass – 6.25%, dense vascularised mass – 6.25%; muscular tissue biopsies: 56% without muscular tissue abnormalities, 30% with a discreet chronic inflammatory process, 14% with an interstitial fibrohyalin zone; histopathologic: 65.38% – follicular thymus hyperplasia with development of germinal centres, majority a 3 Alpert degree; 16.67% – thymomas – predominantly epithelial: 23.07%, predominantly lymphocytic: 30.76%, mixed: 15.38%, spindle cell patterns: 7.69%, thymolipomas: 23.1%; 17.95% – thymic involution and atrophy; good therapeutic response to thymectomy was observed in 63% patients.

**Conclusions:** This study shows the increasing prevalence of MG in later life. Follicular thymus hyperplasia seems to be more frequent in younger women and thymomas in elder men. AchR and other substances that interfere with neuromuscular transmission are important to be determined from a prognostic point of view.

**P2384**  
**PERIPHERAL NERVES INJURY IN THE CENTRAL NERVOUS SYSTEM DEGENERATION: A PILOT STUDY**  
Z.C. Chovancova, I.N. Nestrasil, J.D. Dufek, M.N. Nevrlý, P.K. Kanovsky  
Department of Neurology, Palacky University, Faculty of Medicine, University Hospital, Olomouc, Czech Republic

**Objectives:** Neurodegenerative diseases (NDs) are the largest group of the central and peripheral system disorders. Some of the NDs have a progressive course and they are genetically conditioned.

**Methods:** EMG examination was performed in 42 patients (16 males, 26 females: aged 29–87, mean 65±12 years) suffering from a diagnosed NDs. Common causes of the peripheral polyneuropathy as metabolic, endocrinological and paraneoplastic were excluded.

**Results:** Polyneuropathy was diagnosed in 18 (42.8%) of the 42 patients. The axonal symmetric polyneuropathy of lower limbs was found in 10 patients suffering from Parkinson’s disease. In the one patient suffering from Alzheimer Dementia, light distal symmetric-axonal demyelinating sensory-motor polyneuropathy of the lower limbs with a chronic course was diagnosed. The axonal symmetric polyneuropathy of the lower limbs was found in 3 patients suffering from spinocerebellar ataxia and chronic axonopathy was found in 2 patients suffering from Dementia of Lewy body and one patient suffering from Progressive supranuclear palsy and one patient suffering from Parkinson disease with dementia. Polyneuropathy was not found in the rest of the patients.

**Conclusion:** The peripheral nerve injury was present in the relatively large number of patients suffering from neurodegenerative disorders. However, with respect to a relatively small set of patients, it is rather difficult to clearly establish relationship between individual neurodegenerative disease and EMG determination of the peripheral nerves injury. Further studies performed in a larger set of patients are needed.

**P2385**  
**FIBROMYALGIA RELAPSE EVALUATION AND EFFICACY FOR DURABILITY OF MEANINGFUL RELIEF (FREEDOM) TRIAL: A 6-MONTH DISCONTINUATION TRIAL OF PREGABALIN FOR THE PAIN OF FIBROMYALGIA**  
L.J. Crofford, S. Simpson, J.P. Young, Jr, T. Leon  
¹University of Kentucky, Lexington, KY, ²Pfizer Global R&D, Ann Arbor, MI, ³Pfizer Global Pharmaceuticals, New York, NY, USA

**Objective:** Pregabalin has shown efficacy for reducing pain associated with fibromyalgia. We investigated the durability of pregabalin treatment effect in patients with fibromyalgia.

**Methods:** Randomized, double-blind, placebo-controlled design: 1-week screening; 6-week open-label (OL) (individualized dosage of pregabalin monotherapy; 300, 450, or 600 mg/d); 26-week double-blind (DB). Randomized patients had ≥50% reduction in mean Pain VAS score from OL baseline and Patient Global Impression of Change (PGIC) rating of at least “much improved” at the end of OL and received pregabalin (optimized OL dosage of 300, 450, or 600 mg/d) or placebo. Primary endpoint: time to loss of therapeutic response (LTR), defined as <30% reduction in pain VAS score (from OL baseline) during 2 consecutive visits or subjective worsening of fibromyalgia (e.g., patient needs alternative therapy). Primary analysis evaluated all pregabalin dosages vs. placebo.

**Results:** 1051 patients entered OL; 663 completed; 566 (85%) met DB inclusion criteria and were randomized to pregabalin (n=279) or placebo (n=287). Time to LTR was significantly longer for pregabalin (p<0.0001); 25% of placebo patients had LTR by Day 7, compared with Day 34 for pregabalin patients. Nearly twice as many placebo patients (61%) had LTR by end of DB as compared to pregabalin patients (32%; p<0.0001). The most common AEs during OL were dizziness (36%) and somnolence (22%); during DB, most common AEs exceeding placebo were sinusitis (pregabalin, 5% vs. placebo, 3%) and arthralgia and anxiety (5% vs. 2%).

**Conclusions:** Pregabalin monotherapy demonstrated superior durability of efficacy in fibromyalgia response in this 32-week treatment study.

**P2386**  
**CONDUCTION STUDIES BEFORE AND 3 MONTHS AFTER ENDOSCOPIC CARPAL TUNNEL SYNDROME SURGERY WITH INTRACARPAL PRESSURE MEASUREMENTS**  
E. Ehler, M. Kantza, S. Rehak  
¹Department of Neurology, Regional Hospital, Pardubice, ²Department of Neurosurgery, University Hospital, Hradec Kralove, Czech Republic

Compared with classical midpalmar incision technique the endoscopic approach in carpal tunnel surgery is more careful to skin and equally safe. To be sure that the median nerve decompression is completed in endoscopic approach we used an intracarpal pressure (ICP) sensor for carpal tunnel pressure measurement. During the last 3 years we have inserted ICP sensor made by Codman in 30 patients operated by unipolar endoscopic technique. We have inserted the sensor into different parts of the carpal tunnel (distal antebrachial, proximal, middle, distal carpal tunnel and also palmar space) during the operation and measured the pressure in different hand positions. Median nerve conduction studies were made before and 3 months after the surgery. We have evaluated DML (distal motor latency), amplitude of CMAP (compound...
muscle action potential), amplitude of SNAP (sensory nerve action potential) and SCV (sensor conduction velocity; to index finger, antidiromic). Performed statistical tests showed statistically significant improvement of all 4 nerve conduction parameters after surgery. Then we compared our group of patients with intraoperative ICP measurements with a group operated by endoscopic approach but without ICP measurements. Finally we compared our group with ICP measurements with a group of 30 patients operated by classical midpalmar incision technique. The study was supported by IGA MZ âR 8404-3/2005

P2387
CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY WITH SPINAL ROOT HYPERTROPHY, MIMICKING NEUROFIBROMATOSIS
E. Alexiou¹, I. Markakis¹, G. Theologos¹, G. Gekas¹, P. Davaki²
¹Neurological Department, “Agios Panteleimon” General State Hospital of Piraeus, Nikaia, ²Department of Haematology, General Hospital of Piraeus “Metaxa”, Piraeus, Greece

Objectives: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired disorder resulting from immune-mediated damage to the myelin sheaths of peripheral nerves and spinal roots. In neglected cases of CIDP or in patients with a long history, the repeated bouts of demyelination and remyelination result in gross hypertrophy of nerves, roots and plexuses that rarely may lead to significant diagnostic confusion. We present a patient with CIDP and multiple, bilateral, tumour-like enlargements of the spinal roots, suggesting neurofibromatosis.

Case-History: A 43-year-old female was admitted to our department with a 6-year history of progressive leg weakness and stocking-glove sensory impairment. She presented painless swellings of the lateral cervical regions and atrophy of the hands and calves. On neurological examination she had poor balance, marked weakness of proximal leg muscles and bilateral drop feet. Tendon reflexes were absent. Nerve conduction studies, CSF analysis and sural nerve biopsy were characteristic of CIDP. The patient underwent CT-scans of the chest and abdomen which revealed multiple paraspinal masses in the cervical, thoracic and sacral regions. MR imaging demonstrated that these lesions corresponded to massive enlargements of the spinal roots that were radiologically indistinguishable from neurofibromas. The patient was treated with oral prednisolone and monthly trials of intravenous immune globulin and had a rapid clinical improvement.

Conclusion: Patients with long-standing CIDP that are not receiving treatment may develop massive spinal root hypertrophy that masquerades as neurofibromatosis. Absence of other neurofibromatosis features and fulfillment of CIDP diagnostic criteria can help in the differential diagnosis of these disorders.

P2388
POLYNEUROPATHY ASSOCIATED WITH NON-SECRETORY OSTEOSCLEROTIC MYELOMA. A RARE VARIANT OF POEMS SYNDROME
E. Alexiou¹, I. Markakis¹, M. Xifaras¹, G. Gekas¹, P. Repoussis²
¹Neurological Department, “Agios Panteleimon” General State Hospital of Piraeus, Nikaia, ²Department of Haematology, General Oncological Hospital of Piraeus “Metaxa”, Piraeus, Greece

Objectives: POEMS syndrome is a rare multisystem disorder characterized by peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes. We present a patient with polyneuropathy and other manifestations of POEMS syndrome, in whom diagnostic investigation revealed a vertebral osteosclerotic myeloma in the absence of detectable serum paraprotein.

Case-History: A 55-year-old woman was admitted to our department with a 6-month history of progressive leg weakness and low back pain. Physical examination revealed a palpable liver, darkened skin, hypertrichosis, sclerodactyly and digital clubbing. On neurological examination, she had flaccid paraparesis, clumsiness of hands and distal impairment of touch and pain with relatively preserved deep sensation. Tendon reflexes were absent and plantar responses were silent bilaterally. Electrodiagnostic studies were indicative of a demyelinating motor and sensory polyneuropathy. Repeated testing by serum and urine immunofixation failed to demonstrate a monoclonal paraprotein. Radiographs revealed an osteosclerotic lesion of the eleventh thoracic vertebra. Fine needle aspiration biopsy showed widespread infiltration by plasma cells expressing lambda light chains. On bone marrow biopsy, there was only a mild infiltration by myeloma cells. A diagnosis of non-secretory osteosclerotic myeloma was established and the patient received local radiotherapy, followed by melphalan and prednisone, with moderate improvement.

Conclusion: The early detection of an underlying plasma cell dyscrasia is of major importance for the prognosis as well as the treatment of chronic polyneuropathies. Even when serum protein immunoelectrophoresis is negative, the diagnostic work-up in suspected cases should include a screening for bone lesions with plain radiographs.

P2389
LACOSAMIDE IN LONG-TERM TREATMENT OF PAINFUL DIABETIC NEUROPATHY (DNP)
R. Graf¹, W. Frye¹, J. Simpson¹
¹Cedar Research, Tacoma, WA, ²Schwarz Biosciences GmbH, Raleigh, NC, USA

Objective: Lacosamide is being investigated as an anticonvulsant with analgetic properties.

Background: Lacosamide is a functionalized amino acid that has shown efficacy in animal models for pain and epilepsy.

Methods: In this ongoing, open-label trial, subjects enrolling from one of three preceding trials are titrated to their optimal lacosamide dose (100–600 mg/day) in weekly increments of 100 mg/day before entering a long-term maintenance period when dose adjustments are allowed. Pain is assessed twice daily using an 11-point Likert scale. Patient’s Global Impression of Change in Pain (PGIC) is assessed periodically.

Results: As of the interim analysis cut-off, 451 subjects had received lacosamide; 314 (69.6%) were ongoing, 12 (2.7%) discontinued for lack of efficacy. The mean extent of exposure was 216 days, the maximum was 516 days. Common doses were 400 mg/day (26.4% of subjects) and 600 mg/day (22.0%). The mean pain score was 6.35 at baseline. At the end of titration and after 6, 12, and 18 months in the maintenance phase, it decreased to 2.78, 2.16, 2.33, and 2.28, respectively. After 6 months in the maintenance phase, 96.2% of subjects reported feeling better, 3.8% reporting either no change or worsening. At 12 and 18 months in maintenance, 95.8% and 96.4% of subjects reported feeling better, respectively.

Conclusion: Of the interim analysis cut-off, 451 subjects had received lacosamide; 314 (69.6%) were ongoing, 12 (2.7%) discontinued for lack of efficacy. The mean extent of exposure was 216 days, the maximum was 516 days. Common doses were 400 mg/day (26.4% of subjects) and 600 mg/day (22.0%). The mean pain score was 6.35 at baseline. At the end of titration and after 6, 12, and 18 months in the maintenance phase, it decreased to 2.78, 2.16, 2.33, and 2.28, respectively. After 6 months in the maintenance phase, 96.2% of subjects reported feeling better, 3.8% reporting either no change or worsening. At 12 and 18 months in maintenance, 95.8% and 96.4% of subjects reported feeling better, respectively.

12.4% of subjects discontinued prematurely because of adverse events (AEs). Frequently reported AEs in long-term use included dizziness (19.5%), upper respiratory infection (11.1%), nausea (9.8%), and headache (8.6%).
P2390
NITRIC OXIDE AND CU(II) RATIO IN THE STRUCTURES OF THE DAMAGED PERIPHERAL NERVOUS SYSTEM
D.S. Gusev1, D.G. Zverev1, M.V. Nigmetzanova1, Yu. Chelyshev1
1Department of Histology, Cytology and Embryology, 2Department of the Radiospectroscopy and Quantum Electronics, Kazan State University, Kazan, Russia

Trauma of neurons and neurodegenerative diseases are always accompanied by oxidative stress. Copper is a microelement in the organism which plays a critical role in the nervous tissue. Earlier it was established that copper deficiency results in a dramatic decrease of SOD activity and consequently leads to alteration of antioxidative defence system. Nitric oxide (NO) is a free radical which has a distinctive capability to the reactions due to its physical-chemical properties. On one hand, NO reacts actively with ROS forming peroxinitrite which has marked citotoxicity. At the same time, a hypothesis concerning antioxidative activity of NO and its ability to protect the cells from the oxidative stress by its connection with other free radicals exists. In this study, we have analyzed employing electron paramagnetic resonance with diethyldithiocarbamate as a spin trap the ratio of NO and Cu(II) in the peripheral nerve tissue after injury. After the transection of the rat sciatic nerve NO did not change in DRG L4-L5 for 2 weeks after injury while it increased in the proximal and distal stumps to 5–6 days in 2.5 and 2 times respectively. The concentration of the Cu(II) was diminished by 68.2% in DRG L4-L5 and by 67.49% and 67.76% in the proximal and distal stumps respectively. These results allow us to suggest that 4–6 days after injury are more critical period for DRG neurons because of the most production of NO and decrease of the Cu(II).

P2391
THE RESULTS AND EFFECT OF THYMECTOMY FOR MYASTHENIA GRAVIS
R. Hoofer, O. Zapletalova, I. Woznicova, F. Vlcek
Department of Neurology, University Hospital, Ostrava, Czech Republic

Object: To evaluate the clinical effects of thymectomy (TE) in the treatment of myasthenia gravis (MG). MG is an autoimmune disease mainly caused by antiacetylcholine receptor autoantibodies or by autoantibodies against anti MuSK, anti RyR, anti titin and unknown autoantigenic target(s). TE is a standard treatment for MG.

Methods: 56 patients with MG who underwent TE were reviewed to evaluate the long term effects of TE and analyse the factors influencing outcome. Extended TE was performed on 56 patients with MG, 19 males and 37 females, aged 32 (11–77). Complete remission (CR) was defined as asymptomatic medication free or asymptomatic on low-dose single-drug therapy.

Results: The effects of TE were as follows: According to the Monodens standard the overall effective rate of TE was 75%. The CR rate was 23% (13/56), the improvement rate was 52% (29/56), 9 patients showed no change (16%), and deterioration was seen in 5 patients (9%). With proper treatment, especially early TE, the long-term prognosis is good for SP MG patients.

Conclusion: TE should be performed on most of the MG patients early and actively. TE is recommended as an option to increase the probability of remission or improvement. Ample preoperative care may prevent postoperative myasthenic severe symptoms in the patients with such factors.

P2392
RISK FACTORS IN POLYNEUROPATHY ONSET IN PATIENTS WITH PRIMARY PULMONARY TUBERCULOSIS
A.V. Ivashynka1, S.A. Likachev2
1Department of Neurology, National Research and Clinical Center of Neurology and Neurosurgery, National Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

Object: We observed 80 patients with complicated polyneuropathy among other patients with primary pulmonary tuberculosis. Not only tuberculosis, but some other factors can provoke polyneuropathy development in patients with primary pulmonary tuberculosis. Those factors affect further the clinical course and severity of the disease as well. This study aims to reveal factors affecting polyneuropathy development and clinical course in patients with primary pulmonary tuberculosis.

Methods: The group of patients included 62 males and 18 females between ages 20 to 80. A standardized protocol included: clinical neurological examination, quantitative sensory testing, autonomic-function tests, electrophrenography. Biochemical analyses of blood and urine were taken. The correlation between different factors and the clinical course was evaluated.

Results: The study revealed some factors which proved to cause and influence the clinical course of the disease the most. The risk grows with age. 60% of the group consisted of by people between ages 40 and 60. The incidence and severity of the disease is apparently related to pernicious habits, such as alcoholism (45% of the group) and smoking (79%), and can be aggravated by alimentary hypotrophy (73%), low life standards (46%) and activity of the tubercular process (70%). The results obtained correspond with the severe clinical course of the patients in terms of statistics.

Conclusion: Thus the study indicates that the aggravation of polyneuropathy is associated with alcoholism and smoking, alimentary dystrophy, and unhealthy life style caused by low social status.

P2393
THE EFFECT OF ALLOPURINOL IN PREVENTING TOURNIQUET NEUROPATHY IN RATS
M.O. Jarrahi
Physiology Research Centre, Semnan University of Medical Sciences, Semnan, Iran

Background: Motor nerve conduction velocity (MNCV) changes were studied in a rat’s hind limb after 3 hours of tourniquet application and allopurinol administration. Ischaemic-reperfusion nerve injury has been suggested as the mechanism for post-tourniquet limb paralysis. As allopurinol has been shown to prevent ischaemic-reperfusion process in some tissues. We tested the hypothesis that this drug would reduce tourniquet induced nerve injury.

Material and methods: 30 male Albino Rats (200–250 gr) were chosen and divided randomly into 5 groups. MNCV in animals of control groups were measured one week after beginning of the experiments. Tourniquet control group was checked for nerve conduction velocity, by injecting saline, and applying the tourniquet for 3 hours, 1 week after beginning the experiments. Groups ALLO25, ALLO75 and ALLO50, were injected by 25, 50, and 70 mg/kg allopurinol dissolved in saline and one week after opening the tourniquet. Nerve conduction velocity was measured.

Results and conclusion: Based on this research, we concluded that there was not any significant difference between the mean of MNCV in control and allopurinol groups.
**Results:** HRCT revealed possible thymic tissue in 4 (33.3%) patients in group I and 6 (25%) in group II. 3 of the patients from group II underwent rethymectomy, histopathology did not reveal presence of residual thymic tissue. All of them required additional immunosuppressive treatment after reoperation. Results of HRCT of the mediastinum do not differ between the patients who improved after thymectomy and those who did not benefit from surgery.

**Conclusion:** Rethymectomy does not improve the outcome of the patients with non-thymomatous myasthenia gravis.

Financing: 2P05B04626

---

**P2395**

**RETHYMECTOMY IN PATIENTS WITH NON-THYMOMATOUS MYASTHENIA GRAVIS**

A. Kostera-Pruszczyk, A. Kaminska, M. Dutkiewicz, R. Pacho

1Neuromuscular Unit, Polish Academy of Sciences, Warsaw, Poland

**Background and aim:** Thymectomy is a treatment option for patients with generalized myasthenia gravis (MG). In about 10% of MG patients thymectomy does not induce significant improvement. One of postulated causes is incomplete thymus resection. Therefore some surgeons advocate rethymectomy in such patients. Indications for surgery are usually based on the results of the mediastinum CT scans.

**Material and methods:** 36 patients (27 women), aged 30.7 (range 18–54) with generalized MG without thymoma, were followed-up after thymectomy. Intervention status was estimated according to GMFA recommendations. 12 of the patients were in remission or improved (group I), while 24 patients did not improve after thymectomy, all still had significant bulbar symptoms (class IIIb-IVb MGFA), and 6 had history of myasthenic crisis. Mean acetylcholine receptor antibodies were 9.66 nmol/l in group I and 9.79 nmol/l in group II (p<0.05), all patients were MuSK-negative. The results of high resolution CT (HRCT) of the mediastinum of 36 patients after thymectomy for generalized myasthenia gravis were analyzed.

---

**P2396**

**MUSK-POSITIVE MYASTHENIA GRAVIS IN A POLISH POPULATION**

A. Kostera-Pruszczyk, B. Szylik, M. Dutkiewicz, E. O. Obdrzalkova, P. R. Ressner, R. H. Herzig

1Department of Neurology, 2Department of Internal Medicine, Hypertension and Angiology, Medical University of Warsaw, Warsaw, Poland

**Background and aim:** MuSK-positive myasthenia gravis (MG) is diagnosed in up to 47% of generalized seronegative cases in different populations. Presence of anti-MuSK antibodies is often related to severe bulbar involvement, and no response to thymectomy, although purely ocular cases were also reported. MuSK-positive-MG may also be accompanied by other autoimmune diseases.

**Material and methods:** We tested the frequency and clinical characteristic of MuSK-positive-MG in the Polish population. Sera of 99 patients were tested for presence of antiMuSK antibodies. 51 patients had seronegative-MG (18M, 33F; mean age 36.8, SD 17.7), including 11 with ocular, and 40 with generalized MG. 48 patients were sero-positive (18M, 30F; mean age 33.1, SD 21.3). 3 of the seropositive-MG patients had ocular and 45 – predominantly bulbar symptoms. 10 of seropositive patients had coexistent autoimmune diseases (autoimmune haemolytic anaemia, thrombocytopenia after infectious mononucleosis, Hashimoto thyroiditis, rheumatoid arthritis).

**Results:** All of the patients with seropositive-MG were MuSK-negative. Anti-MuSK antibodies were detected only in 4 patients with seronegative-MG (7.8% of all seronegative-MG, or 10% of generalized seronegative cases): 3 women and one man. Their age at onset ranged from 22 to 40 years. All had generalized symptoms with predominantly bulbar involvement, and underwent thymectomy. Two had respiratory insufficiency before the operation, all required subsequent immunosuppression. They are being followed-up for 2-30 years. All improved clinically, one of the women relapsed after 7 years of remission, none is disabled by the disease.

**Conclusions:** MuSK-positive-MG is rare in a Polish population accounting for 10% of generalized seronegative cases.

Financed with grant 2P05B04626

---

**P2397**

**ACUTE BRACHIAL AND LUMBOSACRAL PLEXOPATHY AFTER INTRAVENOUS SELF-ADMINISTRATION OF HEROIN**

M.G. Kramberger, M. Trost, J. Zidar

1Neurology Department, Teaching Hospital Maribor, Maribor, Slovenia

**Background:** Reports on heroin intoxication related mononeuropathies caused by compression are scarce. The nature of nerve injury in even less commonly recognized conditions, such as plexopathies and polyradiculopathies, remains unknown. They may be due to toxic effects of heroin and/or added substances.
**P2398**

**ALCOHOLIC ACROMUTILATING NEUROPATHY. A CASE REPORT**

A. Kuqo, G. Vypshka, J. Kruja

Service of Neurology, UHC, Tirana, Albania

**Background:** Among principal causes of acrodystrophic neuropathy – i.e., leprosy, diabetes, amyloid neuropathy, hereditary sensory neuropathies – alcoholism is controversial since first descriptions (Bureau et al, 1957) incriminating heavy drinking. In our literature review, we found a study of 38 cases belonging to Western Indian rum abusers, with acrodystrophic neuropathy, that tends however to confirm its etiologic role.

**Case report:** This is a case of a 51-year-old male, truck driver who consumed 250 cc pure alcohol daily for the last 25 years. 9 years ago he was operated for a right L4 – L5 intervertebral disk herniation. It was considered as a back failed surgery, because of persistent pain and paraesthesias in the right leg and some months later in both legs. Since 5 years our patient complained of loss of pain and touch sensitivity with marked paraesthesia – like cold and warm sensations or burning feet. In the last two years dystrophic ulcers and indolent mutilations of foot toes have occurred. The patient had no family history of hereditary sensory – motor neuropathy, no diabetes or other metabolic disorders were described and no other evidence of inflammatory or autoimmune neuropathies. He underwent a detailed laboratory examination and all these aetiologies were ruled out. ENG revealed a pattern of distal demyelinating sensory – motor neuropathy.

**Conclusion:** Our patient seems to have no other aetiologies of chronic indolent acromutilating neuropathies. Alcohol abuse over a long time may be the only etiology of this pathology.

---

**P2399**

**RISK FACTORS OF INITIAL WORSENING INDUCED BY CORTICOSTEROID THERAPY IN MYASTHENIA GRAVIS**

T. Kurokawa¹, M. Mitomi¹, M. Shimamura¹, T. Takahashi², Y. Kuroiwa³

¹Department of Neurology, Yokohama City University Medical Center, ²Department of Neurology, Yokohama City University School of Medicine, Yokohama, Kanagawa, Japan

**Aims:** To assess risk factors of initial worsening induced by corticosteroid therapy in myasthenia gravis.

**Methods:** 27 patients who were administered oral prednisolone for the first time or methylprednisolone pulse therapy against exacerbation in our medical centre from 1999 to 2006, were included. They were administered oral prednisolone as initial dose of 20 mg or 30 mg every second day, then increased by 10mg every three times. We divided the patients into two groups on a basis of whether or not they experienced initial worsening, then examined the differences between two groups with respect to age, MGFA classification, QMG score, bulbar symptoms, and pathology of thymus, respectively.

**Results:** 9 patients (33.3%) underwent initial worsening. Median age was 70 years (range 42–80 years), MGFA classification over IIb 77.8%, median QMG score 18 (range 8–22), bulbar symptoms 88.9%. In the remaining, median age was 51 years (range 26–71 years), MGFA classification over IIb 22.2%, median QMG score 11 (range 3–21), bulbar symptoms 50.0%.

**Conclusions:** Older age, severe and bulbar symptoms were found to be significant clinical predictors of initial worsening induced by corticosteroid therapy in myasthenia gravis.

---

**P2400**

**A CASE OF MIGRANT SENSORY NEURITIS**

E. Lindeck-Pozza, P. Hitzenberger, W. Grisold

Department of Neurology, Kaiser Franz Josef Spital, Vienna, Austria

We report on a 34-year-old, male patient presenting with numbness and exercise induced pains since 2 months in a patchy distribution on the lower extremities. 5 years previously the patient had experienced a similar but less severe episode which remitted spontaneously. Clinical examination revealed hypeaesthesia on light touch in the area of the lateral femoral cutaneous nerve bilaterally, the right superficial peroneal nerve and the left sural nerve. Pains could be elicited in the thighs by hip movements. Motor function and reflexes were normal. Standard motor and sensory nerve conduction velocities were normal as were laboratory investigations. Wartenberg’s migrant sensory neuritis was suspected. In previously described cases of this sensory neuritis radial nerves, lateral cutaneous femoral nerve, saphenous, tibial as well as peroneal nerves are most frequently affected. Clinically a pure sensory, often patchy distribution is characteristic, often stretching of the nerves induces pains. Nerve conduction studies can be normal, however the affected sensory nerves are usually not part of a standard examination. Morphologically the findings from biopsies reported in the literature are heterogeneous. Nerve biopsy is performed in the sural nerve in most patients and may be negative if other sensory nerves are only affected. Although the cause of this neuropathy is unclear, immune mechanisms have been suspected due to morphologic findings of inflammatory infiltrates. A diagnostic procedure should consider nerve biopsy of the affected nerve to confirm inflammatory changes. A spontaneous relapsing and remitting course has been described. Presently only symptomatic treatment of symptoms is considered.

---

**P2401**

**THE EFFICACY OF ALPHA LIPOIC ACID IN TREATMENT OF DIABETES PATIENTS WITH DISTAL SYMMETRIC POLINEUROPATHY (DSP)**

N. Lobjianidze, N. Kvirkvelia, N. Mikava, R. Shakarishvili

Department of Neurology, State Medical University #2 Clinic, Tbilisi, Georgia

**Background:** Distal Symmetric Polyneuropathy (DSP) is the most frequent complication, leading to rising incidence of morbidity,
mortality and increasing of expenses in care of diabetes. According to some studies positive results were reached with alpha lipoic acid in terms of pathogenic treatment approach.

**Objectives:** The aim of the study was the evaluation of action of alpha lipoic acid in diabetes patients with DSP.

**Methods:** 61 patients of both sexes with Type II diabetes mellitus were evaluated. 31 of them made up the study group and 30 – the control group. All study patients were administered Thiogamma (alpha lipoic acid, Worwag Pharma, Germany) during 7 weeks. The efficiency of Thiogamma was evaluated before and at the end of treatment using electromyography data (with machine NOMAD), Neuropathy Symptom Score (NSS), Neuropathy Deficit Scores (NDS). Statistical evaluation was perform by SPSS.

**Results and conclusion:** The analysis carried out has shown statistically valid reduction of scores of DSP symptoms according to NSS during the conduction of the study. After 3 weeks of treatment, the reducing for more then 1 score was noted in 87%, after 7 weeks – in 100%. Thiogamma therapy leads to statistically valid improvement of a vibration sensation in the distal part of lower extremities. Among the ENMG parameters, most frequent is the M-indicators amplitude reduction in the motor nerves (n.peroneus – in 22 (70%) cases, n.suralis – in 12 (38.7%) cases) and decreasing of nerve conduction velocity in sensor nerves (n.peroneus in 12 (38.7%) cases, n.suralis – in 4 (12.9%) cases). Thiogamma therapy improves the general status of patients, their working ability and the tolerance of physical activity rises; accordingly the quality of life also improves.

---

**P2402**

**RECONSTRUCTION SURGERY OF LESIONS OF NERVUS FACIALIS**

V. Matejčík

Department of Neurosurgery, Medical Faculty of Comenius University, Bratislava, Slovak Republic

**Objective:** The study presents the results of reconstruction surgical treatments of lesions of n. facialis with n. hypoglossus and n. accessorius performed in our clinic.

**Patients and methods:** 10 patients were treated by anastomosis of n. facialis with n. hypoglossus (HFA), 1 patient by anastomosis of n. facialis with n. accessorius (AFA). All operations were performed under the microscope; HFA and AFA anastomoses were sutured without tension at perineurium. We did not use end-to-side anastomosis or reconstruction of n.VII-VII in pontocerebellar angle, in pyramid or symmetric anastomoses of n.VII-VII in any of the cases. The results were objecitived by the VI-grade scale Brudny’s modification of House-Brackman classification introduced originally for scaling of the outcome of HFA anastomosis.

**Results:** In all cases HFA and AFA anastomosis the 3rd grade of facial nerve function was reached. Glossal hemiatrophy or atrophy of m. sternocleidomastoideus and m. trapezius was found in patients treated by cross-anastomosis with n. hypoglossus or n. accessorius. In HFA, and even more so expressed in AFA anastomosis in excitation or longer lasting oral communication, there were gentle synkineses in the region of labial angle, chin and lower eye lid.

**Conclusion:** When compared AFA with HFA anastomosis, HFA brings better mimick function and more discrete synkineses. We prefer HFA anastomosis also because the discomfort caused by the atrophy of m. trapezius and m. sternocleidomastoideus was apparently more perceivable in patient treated by AFA than the negative effects of hemiatrophy reported by patients treated by HFA.
by rest or sleep in the day; it had a circadian variation. It resulted in learnt behaviours of pacing and activity avoidance as well as emotional sequelae of frustration and low mood.

**Conclusion:** The fatigue in MG clearly went beyond simple use dependent muscle weakness. There was an interesting and complex relationship between what might be termed peripheral muscle ‘failure’ and a wider symptom of fatigue, which may have biopsychosocial or central components. Further investigation of this relationship and comparison of MG fatigue to the fatigue in other diseases may help to establish possible underlying pathophysiological mechanisms.

**P2405**

**SHORT SEGMENT INCREMENTAL TECHNIQUE: SENSITIVITY AND SPECIFICITY OF DIFFERENT CONDUCTION BLOCK CRITERIA IN ULNAR NEUROPATHY IN THE ELBOW**

S.V. Mosenko
Department of Neurosurgery and Neurology, Odessa State Medical University, Odessa, Ukraine

**Objective:** Electrodiagnostic studies in ulnar neuropathy of the elbow (UNE) using short segment incremental studies (SSIS) and combined recordings from abductor digitii minimi (ADM) and first dorsal interosseous (FDI).

**Methods:** 20 controls and 30 patients with symptoms and signs of UNE were examined, using standard nerve conduction techniques. SSIS were performed in 2 cm extending 4 cm below and 6 cm above the medial epicondyle (D4,D2,C,P2,P4), using ADM and FDI as target muscles.

**Results:** Abnormal slowing was identified in 28 nerves. The mean abnormal latency for SSIS of the ulnar nerve across the elbow for the patient group was 0.78 msec for the ADM and 0.75 msec for the FDI. Motor conduction block was seen in 5 nerves. All nerve segments with abnormal motor conduction velocity across a 10 cm segment of the ulnar nerve at the elbow demonstrated abnormal SSIS, but SSIS were the only abnormalities in 17.9% and 28.6% of ulnar nerve segments across the elbow to ADM and FDI respectively. The site of abnormal segment latency correlated exactly for ADM and FDI in 13 (46.4%) nerves, partially with overlap in 11 (39.3%), and there was no correlation in 4 nerves. The abnormal latency was multifocal in 15 (50%) nerves. The most frequent site of abnormal slowing was retro-epicondylar (6-D2) in 67.9% and 60.7% of nerves for ADM and FDI respectively. Slowing in the most distal segment (D2-D4) was seen in 14.3% and 3.6%.

**Conclusions:** SSIS are sensitive and useful techniques for demonstrating nerve conduction abnormalities and entrapment sites at the elbow.

**P2406**

**SAFETY AND EFFICACY OF PREGABALIN FOR CHRONIC CENTRAL NEUROPATHIC PAIN FOLLOWING SPINAL CORD INJURY (SCI): AN OPEN-LABEL EXTENSION STUDY**

T.K. Murphy, E. Durso-De Cruz, T. Griesing, E. Whalen
Pfizer Inc., New York, NY, USA

**Background and aims:** Pregabalin demonstrated robust efficacy for relief of central neuropathic pain related to SCI in a double-blind, randomized, placebo-controlled trial. We report on the long-term, open-label extension of this trial.

**Methods:** These ≥9-month, open-label extension enrolled compliant patients with no serious treatment-related adverse events (AEs). Patients received pregabalin 150 mg/d (BID) within ≥1 week of concluding double-blind treatment; subsequent dosage adjustment (150-600 mg/d) was allowed to optimize efficacy/tolerability. Quarterly drug holidays lasted 3–28 days depending on when patients relapsed (pain worsening at least “moderately”); patients who did not relapse were withdrawn. Efficacy assessments: Short-Form McGill Pain Questionnaire (SF-MPQ). Safety assessments: AEs, laboratory tests, ECGs, physical exams, oedema assessments, American SCI Association Impairment Scale.

**Results:** 104 enrolled (82.5% men; 96.1% white; mean age=49.8 years), 1 was not treated, 60 completed, 43 discontinued. 51 received double-blind pregabalin, 53 placebo. In the ITT population (ن=102), mean (SD) endpoint improvements in SF-MPQ sensory, affective and total scores were –0.7 (5.8), –0.3 (2.8), –1.0 (8.1); VAS score, –7.9 (25.2); PPI scale, –0.3 (1.2). Endpoint drug-holiday pain assessments (n=88): 43.2% very bad, 27.3% bad, 23.9% little worse, 3.4% moderately, 2.3% not worse. 42 patients (40.8%) had serious AEs; 4 (3.9%) deemed treatment-related; 1 patient died of non-treatment-related cancer. CNS AEs were the most frequent treatment-related AEs, including somnolence (18.4%), dizziness (16.5%), insomnia (10.7%). 15 patients (14.6%) withdrew due to AEs.

**Conclusions:** Long-term pregabalin treatment resulted in further improvements of chronic central neuropathic pain after SCI. The safety profile was consistent with that previously established for pregabalin.

**P2407**

**EFFICACY, SAFETY, AND TOLERABILITY OF PREGABALIN AS TREATMENT OF CHRONIC PERIPHERAL NEUROPATHIC PAIN SYNDROMES: POOLED ANALYSIS OF 11 RANDOMIZED CLINICAL TRIALS IN PAINFUL DPN AND PHN**

T.K. Murphy, J.P. Young Jr, L. LaMoreaux, B. Emir
Pfizer Inc., New York, NY, Pfizer Global Research and Development, Ann Arbor, MI, USA

**Background and aims:** To further elucidate the analgesic effect of pregabalin as treatment for neuropathic pain associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN).

**Methods:** We evaluated pooled data from 11 double-blind, placebo-controlled trials involving 2510 patients (919 received placebo; 427, 496, and 668 received pregabalin 150, 300, and 600 mg/d). The primary efficacy measure was endpoint mean pain score (daily, patient-recorded, 11-point numeric rating scale). Endpoint mean pain-related sleep-interference scores and Patient Global Impression of Change (PGIC) were secondary efficacy measures.

**Results:** Pregabalin-treated patients demonstrated significantly greater pain reductions than those on placebo. Changes from baseline to endpoint in mean pain score were: –1.85, –2.25, –2.64 for pregabalin 150, 300, 600 mg/d vs. –1.24 for placebo (all p<.0001). Similarly, changes from baseline to endpoint in mean pain-related sleep-interference scores were statistically significant (all p<0.0001): –1.84, –2.21, –2.54 for pregabalin 150, 300, 600 mg/d vs. –1.10 for placebo. Significantly greater proportions of pregabalin patients reported “much” or “very much” improvement at endpoint on the PGIC: 56.7%, 66.1%, 79.5% of pregabalin 150, 300, 600 mg/d patients vs. 47.0% of placebo patients (all p≤0.0003). Treatment-emergent adverse events (AEs) were typically mild to moderate (dizziness and somnolence were the most common). AEs led to withdrawals by 13.3% of pregabalin patients and 5.9% of placebo patients, suggesting pregabalin was generally well tolerated by this large population.
Conclusions: Significant improvements in pain and related sleep interference, and patients’ impressions of their health status were associated with pregabalin treatment.

P2408
ATP PREVENTS POST-DENERVATION DEPOLARIZATION OF THE MAMMALIAN MUSCLE FIBERS
N. Naumenko, A. Shakiirizyanova
Normal Physiology Department, Kazan State Medical University, Biophysics of Synaptic Processes Laboratory, Kazan Institute of Biochemistry and Biophysics, KSC, RAS, Kazan, Russia

It has been shown that the motor neuron section leads to the drop of the resting membrane potential (RMP) of muscle. Co-mediator ATP, which is co-released with acetylcholine is one of the active neurotransmission autoregulator. Thus, we have suggested that ATP is also the component of muscle fibres neurotrophic control. It was shown that incubation of rat diaphragm in culture medium at 37°C within 3 hours leads to the drop of RMP. The presence of ATP (100 mM) in bath solution delays the development of postdenervation depolarization. It has been shown in our laboratory that activation of Na+/K+/2Cl– transport is the cause of denervation depolarization development, therefore we suggested that effect of ATP is bound up with this transport activity. The presence of Na+/K+/2Cl– transport inhibitor bumetanide (5 mM) in the culture medium delayed the decrease of RMP (75.7±0.6 mV). Thus ATP and bumetanide hyperpolarized sarcolemma in equal degree. Furthermore, ATP and bumetanide combined application did not lead to the summation of these chemical effects. Denervated muscles RMP in this case was 76.4±0.5 mV and thus did not differ from its significance in the presence of ATP or bumetanide alone and from RMP of the normally innervated fibres. Thus, hyperpolarizing effect of ATP is mediated by the control of Na+/K+/2Cl– transport activity and chloride influx in the muscle cells. It can be concluded, that ATP greatly participates in the mammalian muscle fibres neurotrophic control and is one of the main and very important factors providing the skeletal muscles normal functioning.

P2409
MYASTHENIA GRAVIS ASSOCIATED WITH CASTLEMAN’S DISEASE
Department of Neurology, Eulji University Hospital, Daejeon, South Korea

Castleman’s disease is a relatively rare disease of differential diagnostic interest in patients with lymphadenopathy. The etiology and pathogenesis are still not elucidated. Castleman’s disease can present with localized or disseminated lymphadenopathy; some patients have systemic symptoms. The disseminated form is often accompanied by anaemia and polyclonal hypergammaglobulinaemia. Traditionally, the disease has been classified on clinical grounds (solitary or multicentre) and by histological appearance (hyaline vascular pattern, plasma cell predominance, or mixed lesions). It is now increasingly clear that there are different aetiologies for each of these different subtypes. Reported associations include POEMS syndrome, paraneoplastic pemphigus, Hodgkin’s disease, and follicular dendritic cell sarcoma. One case of Castleman’s disease and myasthenia gravis is reported. A previously healthy, 51-year-old man presented with dysarthria, difficulty in mastication, diplopia, ptosis, and general weakness, and had recently been diagnosed with acetylcholine receptor-positive myasthenia gravis. A computed tomogram (CT) had been performed and revealed a left pararenal mass. At operation the thymus was removed intact. After the pararenal mass was successfully removed, tissue samples were sent for histological analysis. Histologically, the lymph nodes demonstrated the hyaline-vascular type of Castleman’s disease. We present a case of Castleman’s disease associated with myasthenia gravis, the first reported case in the Korean literature. We discuss Castleman’s disease and review the literature.

P2410
BILATERAL CROCODILE TEARS SYNDROME IN THE COURSE OF MELKERSSON-ROSENTHAL SYNDROME: A CASE REPORT
M.K. Owecki, M. Kapelusiak-Pielok, P. Kowal, W. Kozubska
Department of Neurology, University of Medical Sciences, Poznan, Poland

Background and aims: Melkersson-Rosenthal syndrome (MRS) is characterised by a triad of recurrent orofacial swelling, relapsing facial paralysis, and fissured tongue. The classic triad is infrequent, and oligosymptomatic variants are seen more often. Crocodile tears syndrome (CTS) is a rare complication of facial nerve paralysis characterized by inappropriate lacrimation on the side of the palsy in response to salivary stimuli. It results from aberrant reinnervation of lacrimal gland by salivary parasympathetic fibres. We describe the first reported case of the development of bilateral CTS in the course of MRS.

Conclusions: We consider the case deserves attention due to its rarity.

P2411
INTRAVENOUS IMMUNOGLOBULIN TREATMENT IN CHRONIC INFLAMMATORY DEMENTYLATING POLYNEUROPATHY AND MULTIFOCAL MOTOR NEUROPATHY
N. Subutay Oztekin1, M.F. Oztekin2, G. Orhan1, F. Ak1
12nd Neurology Department, 1st Neurology Department, SB Diskapi Education and Research Hospital, Ankara, Turkey

Introduction: In this study we present the results of 8 chronic inflammatory demyelinating polyneuropathy (CIDP) and 6 multifocal motor neuropathy (MF MN) patients treated with intravenous immunoglobulin (IVIG).

Method: The diagnosis of CIDP was based on clinical history, neurological examination, standardized testing including spinal fluid examination, electrodiagnostic studies and nerve biopsy. Immune-electrophoresis was obtained from all patients to exclude monoclonal gammopathy. The diagnosis of MF MN was based on clinical findings, electrodiagnostic studies showing conduction block and biopsy confirmation. Functional assessment was made by MRC and with modified Rankin disability scale as described previously in the text. Strength, sensory testing and rankin evaluations were performed at the initial evaluation and following each course of treatment. All the patients were treated with IVIG 0.4 g/kg/d for 5 consecutive days and repeated at the same dose at monthly intervals for 12 months.

Results: 6 CIDP patients responded significantly to IVIG therapy, 4 of which had complete remission. 2 had incomplete remission, and had relapses after the discontinuation of the monthly therapy. In the MF MN group improvement or stabilization occurred in 4 patients which started 2–12 days after treatment, almost in all patients amyotrophy. 2 cases had no response to treatment and those were the cases with amyotrophy.
P2412
CARDIOVASCULAR AUTONOMIC DYSFUNCTION IN PATIENTS WITH “FLAIL ARM” AND “FLAIL LEG” PHENOTYPES OF AMYOTROPHIC LATERAL SCLEROSIS
M. Tutaj, K. Pasternak, M. Ficek, A. Kyrzyw, B. Tomik, A. Szczudlik
Department of Neurology, Jagiellonian University Medical College, Krakow, Poland

Background and aims: “Flail arm” (FA) and “flail leg” (FL) are rare ALS phenotypes with a distinct clinical course that is sometimes associated with better survival. Cardiovascular autonomic system (CAS) disturbances can negatively affect prognosis in many diseases and have been described in ALS. However, there are no data existing on CAS function in FA or FL. The aim of the study was to compare CAS function in patients with limb-onset (ALS-L) and bulbar-onset (ALS-B) forms of classical ALS with patients with FA/FL phenotypes and to compare CAS function among subgroups of FA/FL patients in whom bulbar, trunk, or limb involvement subsequently developed.

Methods: In 5 ALS patients with FA (2) and FL (3) phenotypes, 6 patients with classical ALS: ALS-L (3), ALS-B (3) and 8 age and gender matched healthy volunteers, we continuously monitored ECG, respiration and blood pressure (BP) during supine rest and head-up tilt. CAS function was assessed based on heart rate (HR), systolic (SBP), diastolic (DBP), and mean blood pressure MBP responses to orthostatic stress.

Results: During head-up tilt, significant falls in BP were observed in ALS-B and in FA/FL with trunk involvement as the second manifestation of the disease, whereas BP remained unchanged in healthy persons, patients with ALS-L, and FA/FL with limb involvement at a different level as the second manifestation.

Conclusions: Sympathetic dysfunction occurs in patients with ALS-B and in a subgroup of FA/FL patients with involvement of the trunk as the manifestation following development of the initial FA or FL signs.

P2413
SLOW DISEASE PROGRESSION AND PROLONGED SURVIVAL IN A PATIENT WITH SPORADIC AMYOTROPHIC LATERAL SCLEROSIS (ALS):
A 28-YEAR FOLLOW-UP
A. Pou-Serradell, J. Royo
1Department of Clinical Neurology, 2Department of Neurophysiological Neurology, Hospital del Mar, Barcelona, Spain

Objective: To analyse the disease, progression in one patient with ALS evolving from the brachial amyotrophic diplegia (BAD) to a definite ALS.

Case report: A 47-year-old man (no affected relatives, left clavicular fracture at 17 years of age) presented with a 28-year history of progressive painless hands, arms and shoulder girdle weakness and later on – in lower limbs, low-amplitude of CMAPs and no conduction blocks. The central motor conduction stimulation was abolished. Cervical MRI was unremarkable in 1987 and showed a moderate spinal cord atrophy in 2007. Serum creatin kinase and genetic testing for mutations in SMN gene were negative.

Results: EMG demonstrated denervation potentials in upper and lower limbs, low-amplitude of CMAPs and no conduction blocks. The central motor conduction stimulation was abolished. Cervical MRI was unremarkable in 1987 and showed a moderate spinal cord atrophy in 2007. Serum creatin kinase and genetic testing for mutations in SMN gene were negative.

Conclusions: Our patient, with the El Escorial criteria for definite ALS, is still alive 28 years after onset. Young age at onset, limb side of onset and longer diagnostic delay may be considered early predictors of prolonged survival in ALS in this case.

P2414
ADULT-ONSET LOWER MOTOR NEURON DISEASE: CLINICAL ANALYSIS AMONG PATIENTS WITH AND WITHOUT DELETIONS ON THE SMN GENE
A. Pou-Serradell, E. F. Tizzano, M. J. Barceló
1Neurology Department, Hospital del Mar; 2Genetic Department, Hospital Sant Pau, Barcelona, Spain

Objective: Establish phenotype-genotype correlation in LMND patients.

Patients: 20 patients with LMND were studied.

Methods: Genetic analysis was performed using RT-PCR. Clinical data: a) Sex b) age at present c) age at disease-onset (decades) d) proximal (P)-symmetrical (S)-asymmetrical (AS) weakness distribution e) calves hypertrophy, f) disease course g) duration of the disease h) presumed mode of inheritance i) sporadic case.

Results: Without SMN gene deletions: (11 patients, 8 families): a) 8M/3F; b) mean: 44 years; c) 3-4; d) D,S:3; P:2, D,P,S:3, D,PAS:1; P,AD:2; e) 1; f) slow: 8, mildly progressive: 3; g) mean: 26 years; h) AD: one, AR: two; i) 5. With SMN gene deletions (9 patients, 5 families): a) 4M/5F; b) mean: 41 years; c) 2-3; d) D,PAS:7; PAR,2; e) 2; f) slow: 4, mildly progressive: 5; g) mean: 31 years; h) AR: three; i) 2.

Conclusions: 1) Deletions are more frequently found in females, young age at disease-onset, P weakness and severe course. 2) Patients without SMN deletions presented as limited forms of symmetrical weakness, chronic and asymmetrical forms and sporadic cases 3) LMND resembling SMA showed frequently SMN deletion.

P2415
DEVELOPMENT OF A CLINICAL PATHWAY FOR THE ATTENTION OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS IN A REGIONAL NETWORK IN MADRID, SPAIN
1Department of Neurology, Hospital Universitario La Paz, 2Department of Neurology, Hospital General Universitario Gregorio Marañón, 3Department of Neurology, Hospital Carlos III, 4Department of Neurology, Hospital Universitario 12 De Octubre, 5Department of Neurology, Hospital Clinico San Carlos, 6Department of Preventive Medicine, Hospital Universitario La Paz, Health Service of Madrid, Spain

Background and aims: Amyotrophic Lateral Sclerosis requires complex multidisciplinary attention. Clinical pathways consist of...
assistance plans for certain diseases with a predictable course, these plans are always established in isolated centres, not in multi-central regions. The aim is to develop a clinical pathway capable of organizing and homogenizing the attention in a regional network which is made up of 5 hospitals, from the beginning until the end of the disease.

**Methods:** During continuous meetings, neurologists of these hospitals and members of the Servicio Madrileño de Salud (Health Service of Madrid), evaluated the therapeutic published guidelines and other documents, used in the attention of ALS. A clinical pathway was developed, adapting this information to social-sanitary conditions in Spain.

**Results:** A clinical pathway was created, consisting of a scientist-technical framework which arranges the attention in relation to the diagnosis, and the treatment, according to the degree of disease progression and a chronogram. The framework is accompanied by various patient-information documents on the disease and the tests that are required, and a patient evaluation form. The standards are established to reach and to promote a constant improvement in patient care.

**Conclusions:** Clinical pathway for the attention of the ALS in a regional network organizes the attention and care that the patient must receive from the beginning to the end of the disease. This arrangement and homogenization of the attention improves the quality of patient care, diminishes the variability in work protocol and rationalizes the use of the sanitary resources.

---

**P2416**

ASSOCIATION BETWEEN SYSTEMIC LUPUS ERITHEMATOSUS AND LAMBERT-EATON MYASTHENIC SYNDROME

J.M. Roriz, R. Morgado, B. Nunes

Neurology Service, Pedro Hispano Hospital, Matosinhos, Portugal

The authors present the case of a 46-year-old woman followed over the last 10 years for an autoimmune picture of spontaneous abortion, thrombocytopenia, small joint arthralgies, Raynaud phenomena, positive ANA and anti-SSa, C4 consumption and positive anti-cardiolipin antibodies – gathering 4 in 11 Hochberg criteria for Systemic Lupus Erithematosus (SLE). After complaining for the last 4 months, about dry mouth, dry eyes, asthenia and gait difficulties, most relevant while climbing stairs or rising from a chair, observation by a Neurologist was requested after she more recently complained of dysphony, solid-dysphagia and small-effort dyspnoea. Examination showed a markedly myopathic gait and predominantly proximal motor deficit, with positive Gowers’ manoeuvre. The EMG established the diagnosis of Lambert-Eaton Myasthenic Syndrome (LEMS) and the patient presented important clinical improvement after IVIG, prednisolone, azathioprine and pyridostigmine. Paraneoplastic etiology was thoroughly excluded by full-body CT, mammary US and X-ray, upper and lower GI endoscopy, laringo-broncho-fiberoscopy, PET-scan and blood tumoral markers. After reasonable response to medication for about 2 months, the patient suffered spontaneous and refractory clinical relapse and ultimately died from aspiration-pneumonia. LEMS is a relatively rare acquired autoimmune channelopathy directed towards pre-synaptic voltage-dependent calcium channels and assumed to be paraneoplastic in over 75% of cases. Even though an increased incidence of connective tissue disease has been traditionally described among non-paraneoplastic cases of LEMS, usually in young females, a surprisingly low number of cases of LEMS associated to LES can be found in NIH/Medline indexed literature over the last 20 years.

---

**P2417**

AMYOTROPHIC LATERAL SCLEROSIS PATIENTS WITH PEG: NUTRITIONAL AND PSYCHOLOGICAL ISSUES

M.C. Tuccio1, P. Bongioanni1, K. Nardi1, F. Tramonti1, M.R. Metelli2, F. Fulceri2, F. Manzone3, B. Rossi1

1Department of Neuroscience, 2Nutritional Service, 3Department of Experimental Pathology, University of Pisa, Italy

**Background:** Patients suffering from ALS often have to face the progressive nutritional problems leading at last to PEG placement.

**Methods:** We evaluated 9 ALS patients with PEG. Many nutritional data has been collected just before and 2 months after PEG insertion, and correlated with disease severity (according to the ALS Functional Rating Scale, ALSFRS). In a subgroup of 6 patients, we studied nutritional data also after 8 months from PEG insertion. A questionnaire was given to caregivers, in order to assess psychological effect of PEG on patients.

**Results:** By comparing the 9 ALS patients before and 2 months after PEG insertion, we found body cell mass index (BCM) mean values significantly (p<0.05) reduced after PEG placement, while plasmatic prealbumin and serum albumin increased, and blood transferrin and lymphocyte counts remained unchanged. Moreover, by considering a subgroup of patients evaluated 2 and 8 months after PEG placement, we found reduced BCM mean values overtime together with increased plasmatic prealbumin, serum albumin and transferrin mean values, whereas lymphocyte counts remained unchanged. More than 50% of patients accepted PEG placement with many difficulties: caregivers also reported patients’ regret not to have accepted PEG before. Only 25% of caregivers reported that PEG influences dependence in activities of daily living.

**Conclusions:** Our results support the concept that PEG placement, although the disease still keeps progressing (as shown by relentless BCM reduction), can improve nutritional status of ALS patients (as shown by enhanced values of plasmatic prealbumin and serum albumin and transferrin).

---

**P2418**

CYTOKINE LEVELS IN SUPERNATANTS OF PERIPHERAL BLOOD LYMPHOCYTES OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

P. Bongioanni1, V. De Tata1, M.R. Metelli2, L. Martino3, F. Fulceri2, F. Manzone3, B. Rossi1

1Department of Neuroscience, 2Department of Experimental Pathology, University of Pisa, Italy

**Background:** In neurodegenerative diseases imbalance between Th1-type cytokines (Interleukin (IL)-2, IL-12, and Tumour Necrosis Factor (TNF)-α) promoting cell-mediated immune responses and Th2-type cytokines (IL-6, and IL-10) modulating humoral responses, might lead to a derangement in immune regulation and apoptosis modulation. The aim of the present study was to assay such molecules in supernatants of peripheral blood lymphocytes (PBL) from patients with Amyotrophic Lateral Sclerosis (ALS).

**Methods:** We used to assay repeatedly overtime plasma concentrations of IL-2, soluble IL-2 receptor (sIL-2R), IL-6, sIL-6R, IL-10, IL-12, TNF-α, sTNF-R1, sTNF-RII in patients with ALS. Disease severity was scored by means of the ALS Functional Rating Scale. Blood samples were drawn in the morning, and plasma was stored immediately at -20°C. PBLs freshly isolated from 23 patients (mean age±SD: 62±11 yrs) were cultured for 3 days and cytokine production in supernatants assayed. Cytokine concentrations were determined quantitatively by enzyme-linked immunosorbent assay.
Results: We found reduced amounts of secreted cytokines in PBL supernatants as compared to cytokine levels in sera from ALS patients. In particular, we assayed more reduced amounts of TNF-α and IL-12, than those of IL-6 and IL-10.

Conclusions: Our findings of significantly decreased amounts of Th1-type cytokines in PBL supernatants from ALS patients might depend on different micro-environment “in vitro” than “in vivo”, so that in the latter PBLs are conditioned to produce more Th1-type cytokines, as they are in a “more toxogenic” environment. Therefore, such data might support the concept of a systemic biochemical and immune derangement in ALS.

P2419
“E_TOOL” FOR NEUROLOGICAL RARE DISEASES SURVEILLANCE: ALS-BARI DATABASE MODEL


1Department of Neurological and Psychiatric Sciences, University of Bari, 2Institute of Biomedical and Pharmacological Research Consorzio Mario Negri Sud, Santa Maria Imbaro, Italy, 3Department of Epidemiology, Harvard University, Boston, MA, USA

Background: The SLA_P Registry (population based registry in Apulia region) is a valid epidemiological opportunity to understand the burden and the regional distribution of the disease and to organize the delivery care network. The Motoneuron Disease Centre of the Department of Neurology of Bari is a favoured observatory of ALS disease since it is the main regional source of ALS patients.

Objective: The aim of the study is to develop a detail diagnostic electronic instrument (“e_tool”) for epidemiological surveillance of ALS in Apulia region in order to increase the SLA_P data with clinical progression markers of disease.

Methods: Incident and prevalent ALS patients have been consecutively inserted in ALS-Bari electronic database.

Results: On February 2007, 95 ALS patients followed at the Motoneuron Disease Centre were entered in the ALS-Bari database. Familial cases of ALS were found in 6 patients (one family multiplex) and of SMA in one patient. SOD1 mutation was identified in 2 patients. At baseline median ALSFRS-R was 28 (range 3–37) and MMT 8.9 (range 1–10). Patients were followed for 13.5 (range 2–98) months. During the follow-up 8 patients died, 12 patients received a non-invasive ventilation, and 5 the PEG.

Conclusions: Our analysis shows an early disease onset in a considerable number of patients, suggesting a possible change in demographic features of the disease or alternatively an earlier diagnostic definition. Nevertheless the time delay from the onset of symptoms to diagnosis was always considerable. The high frequency of familial ALS cases was a suggestive result.

P2420
SURVEY OF DEMOGRAPHIC CHARACTERISTICS OF PATIENTS SUFFERING FROM PERIODIC PARALYSIS WITH HYPOKALEMIA IN ARDABIL

D. Savadi Oskoyi, A. Abedi

1Neurology Department, Faculty of Medicine, Imam Hospital, Tabriz University of Medical Sciences, Tabriz, East Azarbayejan, 2Physiology Department, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

Background: Probably hypokalemia is the most important electrolyte disease in medicine.

Methods: This study was done on 50 patients suffering from hypokalemia from year 2000–2005 and they were assessed on the basis of clinical and laboratory studies. K of serum was measured and questionnaires were filled in.

Findings: From 50 patients, 92% were male. Age range was between 19 and 60 years and mean age was 33.6±9.1 years old. The mean of serum K was 2.73±0.49 mmol/liter. With aging the incidence of hypokalemia increased but most patients were in range 20–40 years old. Incidence time was in night or morning (86%). High carbohydrate food and corticosteroids consumption was seen in 11 patients. There was a recurrence of disease in 21 cases and in 40 patients paralysis was seen in 4 extremities. There was hypertension in 4% of patients and hyperthyroidism was positive in 4 patients. EKG was abnormal in 42 patients induced by hypokalemia.

Conclusion: In spite of international references, the ratio of male/female was high in our study but decreasing of K was high in the female. Hyperthyroidism, intake of high carbohydrates foods and using of Corticosteroids cause this disease. Drug therapy with acetazolamide and oral KCL not only decreased duration of hospitalization but also is effective in treatment of hypokalemia.

Keywords: Hypokalemia – Periodic paralysis – sex – age – Ardabil

P2421
SURVEY OF ENVIRONMENTAL FACTORS IN INCIDENCE OF BELLS Palsy IN ARDABIL

D. Savadi Oskoyi1, A. Abedi1

1Neurology Department, Tabriz University of Medical Sciences, Imam Hospital, Tabriz, East Azarbayejan, 2Physiology Department, Ardabil University of Medical Sciences, Ardabil, Iran

Background and objectives: Bell’s palsy (BP) is a relatively common disease characterized by the sudden onset of unilateral facial paralysis. The facial muscle is paralyzed and patients cannot close the eyes or control their saliva. Incidence-ratio in the world is between 11.5–40.2 patients per 100,000 of population. Factors that affect this disease are not clear.

Methods and materials: In a cross-sectional study in Ardabil province and using a centralized system that contains demographic encounter data, the authors estimated rates, trends, and demographic risk of Bell’s palsy during a 2-year period.

Results: There were 140 incident cases of Bell’s palsy among patients referring to private clinic (total 6500 patients). The crude incidence rate was 2.15. Incidence rates were high in ages between 20–30 years and in females and was higher in cold season than in warm ones and higher in cold statue and in farmer working in warm months (p<0.05).

Conclusion: The results are consistent with hypotheses regarding viral aetologies [e.g., reactivations of herpes simplex] of Bell’s palsy that cold can activate this virus.

Keywords: Bell’s palsy, facial paralysis; season, cold, Ardabil
received NSAI drugs with no positive effect. The subjects with somatic diseases were excluded from this study.

**Results:** The radiological exam in 98% of subjects revealed degenerative-dystrophic disturbances in lumbar spine. In 453 subjects MRI exam revealed disk herniations; among them in 18 cases where pain lateralization did not correlate with disk protrusion direction. In 172 patients MRI exam revealed only vertebral dystrophic changes. All patients in the study underwent epidural corticosteroid injections. In 375 subjects pain severity decreased after first injection by 30–40% or 3–4 points according to VAS. In 78 patients any positive results were obtained by epidural injections. CT exam in this group of patients with pseudoradicular syndromes revealed intravertebral joint facet syndromes in 5 patients; the sacroiliac joints pathology in 46 patients; the piriformis muscle syndrome in 11 patients; the coxofemoral joints pathology in 9 patients. In 7 patients EMG exam revealed peroneus nerve tunnel syndrome.

**Conclusions:** The lumbar spine disk herniations and protrusions MRI confirmed, associated with radicular type, pain irradiation is not mandatory the etiological cause of the algic syndrome. The epidural corticosteroid injections may be useful in the differential diagnosis of the nerve root compression caused by vertebral column structures and pseudoradicular syndromes.

---

**P2423**

**THE RELATIONSHIPS BETWEEN SLEEP AND PAIN IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHIC PAIN: RESPONSES TO TREATMENT WITH DULOXETINE**

D.A. Fishbain1, J. Hall2, A. Meyers2, J. Gonzales2, V. Whitmyer2, H. Thompson2, V. Skljarevski2, C. Mallinckrodt2

1Department of Psychiatry and Behavioural Sciences, University of Miami School of Medicine, Miami, FL, 2Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA

**Background:** Data from clinical trials of duloxetine in patients with diabetic peripheral neuropathic pain (DPNP) was used to investigate associations between pain and sleep.

**Methods:** Data was pooled from 3 double-blind, randomized, placebo-controlled, 12-week trials of patients with DPNP in which major mood disorders were excluded. Studies 1–3 (n=342, n=334, and n=348) compared duloxetine 60 mg QD and 60 mg BID with placebo. Efficacy measures included average daily and night pain severity (collected via patient diaries), and the Brief Pain Inventory (BPI) interference items. Weekly mean scores of the daily and night pain severity were calculated for Weeks 1–12. BPI was administered at Weeks 4, 8, and 12.

**Results and conclusions:** At baseline, both daily and night pain severity were positively and significantly correlated with sleep interference (r=0.37 and 0.57, respectively; p<0.001). Both doses of duloxetine were significantly superior to placebo in reducing daily and night pain at Week 1 and at all assessment times thereafter. Placebo response was greater on sleep interference than for either pain measure. Both duloxetine doses were superior to placebo in reducing sleep interference at Week 12. Correlations between changes to endpoint in daily and night pain with sleep interference changes were 0.48 and 0.53, respectively (p<0.001). Results suggest moderate to strong associations at baseline between daily pain, night pain and sleep interference, as well as between changes in pain (daily and night) and changes in sleep interference. Although causality was not established, these findings suggest improvements in pain will be associated with less interference in sleep.

---

**P2424**

**Abstract cancelled**

**P2425**

**THYMECTOMY IN 347 MYASTHENIA GRAVIS PATIENTS (1990–2006)**

P. Spalek1, M. Schnorrer2, K. Sitrova1

1Centre for Neuromuscular Diseases, University Hospital Ruzinov, 2Department of Surgery, University Hospital, Bratislava, Slovak Republic

**Background:** 347 myasthenia gravis (MG) patients (n) were indicated for thymectomy (TE) from 1990 to 2006 (307 p. prior to the age of 50 years, 40 MG p. with thymoma). Indicated for TE were p. either asymptomatic or with mild MG symptoms. These conditions were achieved by immunosuppressive (IS) therapy in 261 p. (75.3%), by IS therapy, plasmapheresis and/or IVIg in 19 p. (5.5%) with weakness of respiratory and/or bulbar muscles and only by symptomatic treatment with anticholinesterases in 67 p. (19.2%). Aim of the study was to established statistical significance of clinical and laboratory findings for beneficial outcome of TE in MG.

**Methods:** All TE were performed by median sternotomy. Average follow-up after TE was 7.3 years. We evaluated the outcome of TE in MG to age, sex, duration of MG prior diagnosis/therapy, thymic pathology and autoantibodies to acetylcholine receptors (AChRs).

**Results:** Clinical remission was achieved in 193 p. (55.6%), pharmacological remission with maintenance IS therapy in 47 p. (13.6%), improvement with maintenance IS therapy and anti-Cholinesterases in 106 p. (31.5%), death in 1 p. (0.3%). We found histologically hyperplastic thymus in 226 p. (63.9%), atrophic thymus in 81 p. (23.1%) and thymomas in 40 p. (13.0%).

**Conclusion:** Age under 40 years, hyperplastic thymus, duration of MG less than 6 months prior diagnosis/therapy, seropositive MG to AChRs were statistically significant factors in beneficial outcome of TE in MG.

**P2426**

**FAMILIAL AMYLOID POLYNEUROPATHY ASSOCIATED WITH THE TRANSTHYRETIN CYS 114 GENE IN A RUSSIAN KINDRED**

I.A. Strokov1, G.M. Dukova1, A.P. Pogromov2, E.V. Generozov3, P.M. Zhdanin4, M.O. Kovalchuk5

1Department of Neurology, 2Department of Gastroenterology, Moscow Medical Academy, 3Institute of Physic-Chemical Medicine, Moscow, Russia

**Background:** Familial amyloid polyneuropathy (FAP) associated with the mutant transthyretin (TTR) gene Cys 114 is a rare pathology and has only been described in one Japanese and one Dutch family.

**Patients and methods:** The family history over four generations revealed 3 affected members with autosomal dominant inheritance. Clinical analyses, DNA diagnosis, EMG, QST, QAT were performed in five patients of 2 generations (monozygotic twins and three of their children).

**Results:** Mutant TTR Cys 114 gene was identified in 4 family members. Amyloid deposition was confirmed in two patients (twins) by rectal biopsy. Only one twin had clinical features which included severe autonomic polyneuropathy (orthostatic hypotension, sexual impotence, diarrhoea, sluggish pupils, constant tachycardia, foot hypohidrosis) and axonal sensory small fibres polyneuropathy with mild motor involvement. The patient had
vitreous opacity, palsy of both VI nerves, and transient sensory and speech disorders. The ultrasound heart examination showed amyloid restrictive cardiomyopathy. Histological findings revealed amyloid deposition in the postbulbar part of the duodenum, terminal part of the intestine, in the rectum and also in sural nerve. MRI (1.5T) showed no pathology.

**Conclusion:** FAP associated with mutant TTR Cys 114 gene in a Russian family is clinically manifested after 45 years by typical autonomic and somatic polyneuropathy, vitreous opacity, heart and intestine features.

**P2427**

**VIBRATION AND TEMPERATURE PERCEPTION THRESHOLD IN PATIENTS WITH TYPE-1 DIABETES – A PRELIMINARY REPORT**

S. Szczyrba, B. Wolnik, G. Kozerà, L. Bieniaszewski, W.M. Nyka
1Department of Adults Neurology, 2Department of Hypertension and Diabetics, Medical University of Gdańsk, Poland

**Background:** Diabetic polyneuropathy (DPN) increases the risk of sudden cardiac death and disability in patients with diabetes. Increase of vibration (VPT) and temperature perception threshold (TPT) is among the first symptoms of DPN. Early detection and therapy for DPN is especially important in young patients with type-1 diabetes, due to possible decrease of life quality in the future. Quantitative sensory testing (QST) of VPT and TPT is regarded as a reliable method for early diagnosis of DPN. The aim of our study was to assess the VPT and TPT in young individuals with and without diabetes using the QST.

**Methods:** 14 patients with type-1 diabetes (mean age 34.14±8.30; mean diabetes history 14.7 years) and 22 individuals without any disorders (mean age 26.72±4.10) underwent a QST examination. With use of Vibratron II and NTE-2 Thermal Sensitivity Tester VPT and TPT in upper and lower extremities were measured.

**Results:** VPT was within normal range in upper and lower extremities, similar in diabetic and healthy individuals (p>0.05). We found a higher TPT in lower extremities in diabetic patients comparing to healthy subjects (3.46 vs. 2.89 SD, regarding normal values; p<0.05). There was no difference in the TPT in upper extremities between diabetic and healthy subjects (p>0.05).

**Conclusions:** VPT and TPT reveal differences between studied groups of diabetic and non-diabetic individuals, even within normal range of function of the nerves. This could be helpful in detection of diabetic neuropathy at its early stage and in prevention of diabetic complications.

**P2428**

**FULMINANT NEUROPATHY MIMICKING CEREBRAL DEATH: A CASE REPORT**

P. Taba, S.M. Luus, L. Puksa, M. Liik
Department of Neurology and Neurosurgery, University of Tartu, Estonia

**Background and aims:** Guillain-Barré syndrome may rarely present as a locked-in syndrome with severe acute tetraparesis and cranial nerve involvement. We describe a case of fulminant neuropathy initially mimicking cerebral death.

**Methods and results:** A 44-year-old woman was hospitalised in the neurointensive care unit with flaccid tetraparesis and absent tendon reflexes, wide pupils without light reflex, missing oculocephalic reflex and respiratory arrest. There were no facial, ocular, or laryngeal movements. Magnetic resonance imaging was normal. Electroencephalography revealed diffuse continuous slowing of background activity in the theta range with amplitude of 30–50 μV, preserved posterior rhythm and photic-driving response. Nerve conduction studies showed no motor and sensory responses after the 3rd day. On day 21st, needle electromyography was performed, active denervation potentials (positive sharp waves and fibrillation potentials) were obtained in cranial, distal and proximal hand muscles, and no voluntary activation in any muscle. The findings revealed acute axonal motor and sensory degeneration. The patient was treated with artificial ventilation, infusion and other intensive care methods, and intravenous immunoglobulin during five days. On the 8th day after admission, the patient was able to demonstrate first signs of conscious response by nodding her head. Some days later, she started to open the eyes. Three weeks after hospitalisation, she could breathe, open the mouth, and move the eyes and the tongue.

**Conclusions:** Though the clinical features indicated cerebral death, EEG excluded the possibility of brain death, and electrodiagnostic evaluation revealed the diagnosis of a peripheral neuropathy.

**P2429**

**SEX HORMONES IN YOUNG PATIENTS WITH SPORADIC AMYOTROPHIC LATERAL SCLEROSIS**

A.V. Vasiliev, M.N. Zakharova
Neuroinfection Department, Institute of Neurology, Russian Academy of Medical Science, Moscow, Russia

**Aim:** The aim of our study was the research of sex hormones in young patients (under 40 years old) with amyotrophic lateral sclerosis (ALS).

**Methods:** 23 young ALS patients (mean age was 33 years) and a control group, consisting of 20 elderly ALS patients (mean age 57 years), were included in the study. Level of sex hormones in plasma was measured by immunochemical assay. All patients were rated according to ALSFRS scale.

**Results:** There was no difference in levels of testosterone, free testosterone, progesterone, 17-OH-progesterone, estradiol, LH, FSH and DHEA-S between young (14 patients) and elderly (7 patients) men. Level of sex hormone binding globulin (SHBG) was significantly decreased, and level of dihydrotestosterone and androstenediol significantly increased in young men. 12% of young men had notably higher level of dihydrotestosterone compared to the rest of young patients. The former had milder course and slower progression of the disease. There was no difference in levels of testosterone, dihydrotestosterone, androstenedione, estradiol, LH, FSH and SHBG between young (9 patients) and elderly (13 patients) women. Level of free testosterone, androstenediol, progesterone, prolactin and DHEA-S was significantly increased in young women. 44% of young women had notably higher level of androstenediol and 22% notably higher level of LH compared to the rest of young patients. The former had a more prolonged course of the disease.

**Conclusion:** Our results suggest that sex hormones play an important role in pathogenesis of ALS.

**P2430**

**QUALITY OF LIFE IN PATIENTS WITH MYOTONIC DYSTROPHY: ASSESSMENT WITH MOS SF-36**

L.R. Akhmadeeva, B.A. Veytsman, Kh.P. Derevyanko, E.N. Zakirova
1Department of Neurology and Medical Genetics, Bashkir State Medical University, Ufa, Russia, 2School of Computational Sciences, George Mason University, Fairfax, VA, USA
P2431

A DIABETIC NEUROPATHY FOLLOW-UP OVER TWO PERIODS OF TIME
A. Alajbegovic1, S. Alajbegovic2, E.M. Suljic1, H. Resic1
1Neurology Clinic, Clinical Center Sarajevo, 2Cantonal Hospital Zenica, 3Center for Hemodialysis, Clinical Center Sarajevo, Bosnia-Herzegovina

P2432

CORELLATION BETWEEN ANXIETY, DEPRESSION AND P-300
S.I. Harbuzau, V.V. Ponomarev, S.V. Vlasova
1Neurological Department, Hospital 15, Minsk, Belarus

P2433

Abstract cancelled

P2434

NATURAL HISTORY OF CERVICAL AND TRUNCAL ONSET OF AMYOTROPHIC LATERAL SCLEROSIS
G.N. Levitsky, A.P. Smirnov, N.I. Levitskaya, V.I. Skvortsova
Department of Fundamental and Clinical Neurology, Russian State Medical University, Moscow, Russia

P2435

THE ROLE OF DICLOBERL IN THE TREATMENT OF RADICULOPATHIES OF VERTEBROGENESIS
Y.N. Madjidova, A.A. Bukreev
Neurology Department, Tashkent Medical Academy, Tashkent, Uzbekistan

P2436

Abstract cancelled

P2437

SERUM CREATINE KINASE (CK) AND MYOGLOBIN VALUES IN AMYOTROPHIC LATERAL SCLEROSIS PATIENTS
M. Ostrowska, D. Zawislak, B. Tomik, A. Szczudlik
Department of Neurology, Jagiellonian University Medical College, Krakow, Poland

P2438

DIAGNOSTIC DIFFICULTIES IN LATE ONSET ACID MALTASE DEFICIENCY (POMPE DISEASE)
N. Subutay Oztok1, M.F. Oztok1, G. Orhan1, F. Ak1
12th Neurology Department, 21st Neurology Department, SB Diskapi Education and Research Hospital, Ankara, Turkey

P2440

INITIAL RESEARCH IN TREATING AMYOTROPHIC LATERAL SCLEROSIS BY PREPARATION OF DELTA-SLEEP INDUCING PEPTIDE
V. Voitenkov, E. Borisova
Clinic and Institute of Experimental Medicine, Saint-Petersburg, Russia

Multiple Sclerosis

P2441

EXPRESSION OF CXCR1 AND CXCR2 IN PBMC OF PATIENTS WITH MULTIPLE SCLEROSIS TREATED WITH MITOXANTRONE
B. Bielecki1,2, T. Berkowicz2, A. Glabinski1,2
1Department of Experimental and Clinical Neurology, 2Department of Neurology, Medical University of Lodz, Poland

Background and aims: Chemokines and chemokine receptors are responsible for direction of migration of various cell types in physiological and pathological conditions including inflammatory and autoimmune diseases like multiple sclerosis (MS). Chemokine receptors CXCR1 and CXCR2 are expressed over a wide range of cell types including T-cells, monocytes and neutrophils. Mitoxantrone (Mtx) is an antineoplastic agent that inhibits the proliferation of T-cells, B-cells and macrophages. It is currently approved for treatment of patients with progressive forms of MS. The aim of this study was the analysis of expression of CXCR1 and CXCR2 in peripheral blood mononuclear cells (PBMC), isolated from healthy donors, MS patients without any immunomodulatory treatment, patients with MS treated with methylprednisolone and patients with MS analyzed at different stages of treatment with Mtx.

Methods: Expression of mRNA was analyzed using quantitative RNase Protection Assay (RPA) technique. The correlation between the disease progression measured with Expanded Disability Status Scale (EDSS) and expression of CXCR1 and CXCR2 in PBMC was also studied.

Results: We observed significant increase of CXCR1 and CXCR2 expression in PBMC of patients with MS. Expression of CXCR1 and CXCR2 in patients treated with methylprednisolone was also significantly elevated but expression of CXCR2 in patients treated with Mtx was significantly diminished. There was positive correlation between the expression of CXCR1 and CXCR2 in PBMC and EDSS in patients with MS without treatment.

Conclusions: Our results suggest a possible role of CXCR1 and CXCR2 in development of MS and indicate that these receptors as possible markers of disease progression.
**P2442**

**AN EXAMINATION OF THE RESPONSE SHIFT PHENOMENON IN RELATION TO THE SELF REPORTED MULTIPLE SCLEROSIS IMPACT SCALE (MSIS-29) IN MS PATIENTS**

L. Costelloe1, K. O'Rourke1, C. McGuigan1, C. Walsh1, N. Tubridy2, M. Hutchinson1
1St. Vincent’s University Hospital, 2Department of Statistics, Trinity College Dublin, Ireland

**Background:** The MSIS-29 is a psychometrically developed, MS specific, patient reported instrument. Response shift is an intrinsic aspect of self-report measures, which may limit their validity longitudinally.

**Aims:** To perform an examination of the response shift phenomenon in relation to the physical and psychological components of the MSIS-29.

**Methods:** 367 MS patients (EDSS 0-8.5) had concurrent EDSS and MSIS-29 assessments over four years. 211 patients had significant EDSS change and 156 patients were stable at follow-up. Patients were stratified into high (EDSS=5.5+) and low (EDSS<5.5) disability levels. MSIS-29 physical and psychological scores were examined at baseline and follow-up using paired T tests. Correlations of change and effect sizes (ES) were calculated.

**Results:** Baseline correlation and correlation of change between the MSIS-29 physical and psychological were moderate (r=0.55 and r=0.52 respectively). Mean MSIS-29 physical scores worsened over time in all patients except in stable patients with high disability (EDSS=5.5+), in whom the MSIS-29 physical score improved by 3.41 points (ES=-0.17). Mean MSIS-29 psychological scores worsened in all changed patients, and improved in all stable patients regardless of disability. Effect sizes were moderate.

**Conclusions:** Response shift has been demonstrated for the MSIS-29 physical in more disabled MS patients with a stable course, and MSIS-29 physical and psychological were moderate (r=0.55 and r=0.52 respectively). Mean MSIS-29 physical scores worsened over time in all patients except in stable patients with high disability (EDSS=5.5+), in whom the MSIS-29 physical score improved by 3.41 points (ES=-0.17). Mean MSIS-29 psychological scores worsened in all changed patients, and improved in all stable patients regardless of disability. Effect sizes were moderate.

**Methods:** Baseline correlation and correlation of change between the MSIS-29 physical and psychological were moderate (r=0.55 and r=0.52 respectively). Mean MSIS-29 physical scores worsened over time in all patients except in stable patients with high disability (EDSS=5.5+), in whom the MSIS-29 physical score improved by 3.41 points (ES=-0.17). Mean MSIS-29 psychological scores worsened in all changed patients, and improved in all stable patients regardless of disability. Effect sizes were moderate.

**Conclusions:** Response shift has been demonstrated for the MSIS-29 physical in more disabled MS patients with a stable course, and MSIS-29 physical and psychological were moderate (r=0.55 and r=0.52 respectively). Mean MSIS-29 physical scores worsened over time in all patients except in stable patients with high disability (EDSS=5.5+), in whom the MSIS-29 physical score improved by 3.41 points (ES=-0.17). Mean MSIS-29 psychological scores worsened in all changed patients, and improved in all stable patients regardless of disability. Effect sizes were moderate.

**P2443**

**ALTERATION IN BLOOD VESSEL DENSITY IN MULTIPLE SCLEROSIS LESIONS IMPLIES A ROLE IN BRAIN SCARRING**

N.J. Gutowski1, J.E. Holley1, P. Eggleton1, J. Whatmore1
1Department of Neurology, Royal Devon and Exeter Hospital, 2Peninsula Medical School, Exeter, UK

The dynamic processes involved in the development of multiple sclerosis (MS) lesions culminate with chronic glial scarring which inhibits repair. Astrocytes, which constitute the main cell type in the glial scar, have a characteristic scar phenotype which is different from quiescent or reactive astrocytes. During normal wound healing, angiogenesis (the formation of new blood vessels from pre-existing vessels) takes place to restore vascular integrity in areas undergoing repair. However, in diseases where damage and repair are ongoing, erratic angiogenic signals might influence scar deposition. Previous preliminary data suggested a change in blood vessel density in MS. This study extended former work by investigating blood vessel density in blocks of post-mortem cerebral white matter from 8 normal control (NC) (n=9 blocks), and 27 MS cases. MS blocks were classified as normal appearing white matter (NAWM) (n=10), acute (n=9), subacute (n=9) and chronic (n=12) lesions by triple label immunohistochemistry. Blood vessel density was quantified by counting vessels in 3 random fields from NC, NAWM and MS lesions. Statistical analysis of the results confirmed alterations in the numbers of blood vessels in the different stages of lesion development. This might indicate that angiogenesis could be an important factor in scarring in MS.

**P2444**

**THE BEGIN STUDY: ASSESSMENT OF PHYSICAL ACTIVITY, FATIGUE AND HEALTH-RELATED QUALITY OF LIFE IN THE EARLY STAGES OF MULTIPLE SCLEROSIS**

M. Hagstromer1, M. Sjostrom1, E-M. Wicklein1, M. Daumer2, I.K. Penner3, M. Tihorec4
1Department of Biosciences and Nutrition, Karolinska Institutet, Stockholm, Sweden, 2Bayer Schering Pharma AG, Berlin, 3Sylvia Lawry Centre for Multiple Sclerosis Research, München, Germany, 4Department of Cognitive Psychology, University of Basel, Switzerland, 5Department of Neuroimmunology, Hospital Vall D’Hebron, Barcelona, Spain

**Background:** Physical activity (PA) has been shown to reduce the risk of several diseases. Results from controlled trials suggest that exercise therapy can be beneficial for MS patients outside exacerbations (Cochrane analysis). Unfavourably in MS, physical disability and fatigue contribute to lowered patient participation in PA. The BEGIN study (Betaferon® treatment and Exercise data Gathering in early MS) is a prospective international multicentre observational study, which will assess PA, fitness, fatigue and HRQoL in patients in early stages of MS, including clinically isolated syndrome suggestive of MS (CIS). The interactions of these parameters will be studied and compared with healthy controls.

**Methods:** BEGIN will include patients with CIS and patients diagnosed with relapsing-remitting MS in the 12 months prior to recruitment, who have begun treatment with interferon beta-1b. Recruitment is expected to be complete in QIII/2008. The target cohort size is 1,000 patients at 200–300 centres worldwide. PA will be measured with an accelerometer (subset of patients), a pedometer and the International Physical Activity Questionnaire. The Fatigue Scale for Motor and Cognitive functions will be applied to assess fatigue, and the EuroQol questionnaire to assess HRQoL. Prevalence of depression will be evaluated using the Center for Epidemiological Studies Depression Scale. CIS will be classified into monofocal or multifocal according to symptoms and signs at presentation.

**Results and conclusions:** The results of this study are expected to give valuable insights into level and pattern of PA, fatigue and HRQoL in patients with early-stage MS, and how these factors correlate with disease activity.

**P2445**

**COMPARISON OF CHILDHOOD AND JUVENILE ONSET MULTIPLE SCLEROSIS WITH ADULT ONSET MS CONCERNING CLINICAL AND MAGNETIC RESONANCE IMAGING FINDINGS**

S. Ozakbas, D. Tosun, E. Idiman
Department of Neurology, Dokuz Eylul University, Izmir, Turkey

**Background and aims:** In 1.2% 6% of multiple sclerosis (MS) cases, the onset of disease is before 16 years of age. Diagnosis of the patients with low age of onset is one of the main questions in childhood onset MS. It is aimed at comparing the childhood and juvenile onset MS with adult onset MS on the basis of clinical and magnetic resonance imaging findings and cognitive impairment.
Methods: 44 patients with childhood onset MS were compared with 64 adult onset patients. Cognitive functions were also evaluated and followed-up. Patients were also compared on the basis of magnetic resonance imaging (MRI) data in the follow-up period.

Results: Mean age at disease onset was 11.8 years in childhood onset group. Diplopia and sensory disturbances were the most common initial manifestations. 57% had a relapsing-remitting course. On the last evaluation, the Expanded Disability Status Scale (EDSS) score was above 5 in 11 patients, and it was below 5 in 21 patients. Cognitive scores worsened in childhood onset in the fifth year (p=0.03). There were more Gd-enhanced lesions in adult onset group (p=0.02) at baseline and in the fifth year (p=0.03). No difference was demonstrated on the basis of either T2 lesions or T1 hypointense lesions between the groups.

Conclusions: Childhood onset MS does not significantly differ on a basis of clinical manifestation, but it seems to have better prognosis regarding MRI parameters. A worse prognosis of cognitive impairment and probably immunological process is less active in childhood onset MS.

P2446

IN VITRO EFFECTS OF INFLAMMATORY CYTOKINES ON NEURAL STEM CELL MIGRATION

A. Kalpatsidis1, L. Zanotti2, E. Dimitriadi3, P. Boura1, K. Kapinas2, I. Milonas2
1Department of Neurology A', Aristotle University of Thessaloniki, Ahepa Hospital, Thessaloniki, Greece, 2Neuroimmunology Unit, Dibi San Raffaele Scientific Institute, Milan, Italy, 3Department of Clinical Immunology, Aristotle University of Thessaloniki, Ippokrateio Hospital, 4Department of Neurology C', Aristotle University of Thessaloniki, Papanikolau Hospital, 5Department of Neurology B', Aristotle University of Thessaloniki, Ahepa Hospital, Thessaloniki, Greece

Background and aims: Selective mononuclear cells infiltration leading to demyelination and axonal damage occurs within the central nervous system (CNS) of patients with multiple sclerosis (MS). This process is mediated by interactions – at the blood-brain barrier (BBB) – of adhesion molecules and counter-receptors. In parallel, chemokines selectively attract inflammatory cells from the periphery towards the inflamed areas of the CNS, thus amplifying the inflammatory process. Several recent studies suggest that inflammatory signals may exert a certain influence on proliferation, migration and differentiation of endogenous stem cells residing within brain germinal niches. Inflammatory cytokines and chemokines have been shown to play a role in directing the migration of neural progenitors in both the developing brain as well as in the peripheral nervous system.

Methods: In our study we have explored the role of inflammatory cytokines in directing the migration of neural stem/precursor cells in vitro. Neural progenitor cells were isolated from neonatal C57Bl/6 mice and pro-inflammatory (IFNα, IL-2, TNFα) or anti-inflammatory cytokines (IL-4, IL-10) were studied for their effects on both cytokinesis and chemotaxis.

Results: Interestingly, both pro- and anti-inflammatory cytokines down regulated the cytokinesis of NPCs, with TNFa being the sole exception, as shown through a modified Boyden’s chamber system.

Conclusions: Pro- and anti-inflammatory cytokines seem to be involved in cytokinesis and migration of neural progenitor and neural stem cells. Further in vivo studies will be needed to clarify the timing and the reciprocal interactions between different inflammatory mediators in regulating the endogenous brain stem cell compartment’s behaviour in CNS inflammatory diseases.

P2447

A PHYSICIAN SURVEY ON TREATMENT SITE AND PRACTICE-RELATED FACTORS AFFECTING ADHERENCE TO DISEASE-MODIFYING THERAPIES FOR MULTIPLE SCLEROSIS

V. Devonshire1, Y. Lapierre2, R. Macdonell3, C. Ramo Tello4, F. Patti5, P. Fontoura2, L. Suchet1, R. Hyde1, I. Bulla1, B.C. Kieseier1, E.M. Frohman1
1MS Clinic, University of British Columbia Hospital, Vancouver, BC, 2Hopital Neurologique De Montreal, Montreal, QC, Canada, 3The Austin Hospital, Heidelberg, VIC., Australia, 4Servicio de Neurologia, Hospital Universitario Germans Trias I Pujol, Barcelona, Spain, 5Policlinico di Catania, Catania, Italy, 6Servicio de Neurologia, Hospital Sao Bernardo, Setubal, Portugal, 7Cabinet Medical, Marseille, France, 8Biogen Idec International GmbH, Zug, Switzerland, 9UT Southwestern Medical Center at Dallas, TX, USA, 10Department of Neurology, Heinrich-Heine University, Düsseldorf, Germany

Background and aims: To determine location and practice-related factors affecting patient adherence to disease-modifying therapies (DMTs) for relapsing-remitting multiple sclerosis (RRMS).

Methods: Patients ≥18 years old with RRMS and on DMT for ≥26 months were included in the observational Global Adherence Project conducted at 176 centres. Physicians completed a questionnaire on their practice, infrastructure, nurse roles, and treatment paradigms. Questions regarding disease, education and adherence factors were asked. Patients who did not miss an injection or change dose in the last 4 weeks were considered adherent.

Results: Of 2,566 patients studied, 75% were adherent to treatment. A majority of participants were seen at dedicated MS centres (66.1%) in central city locations (69.2%). The type (P=0.056), but not location (P=0.137) of treatment site was related to patient adherence. Overall, 74% of sites had a nurse in the practice, and more adherent (80.3%) than non-adherent patients (76.8%; P=0.057) had nurses available. More time was spent with adherent than non-adherent patients at diagnosis (p=0.055). Most physicians (67.4%) were concerned about therapy adherence, citing adverse treatment effects, relapse and disability efficacy, and injection frequency and administration as the most important issues to discuss with patients when choosing therapy. Significantly more physicians discussed adherence at treatment initiation with adherent patients than non-adherent patients (p=0.0004). Where possible, results will be compared with the patient’s perspective.

Conclusions: Discussion of adherence at treatment initiation was a significant factor affecting treatment adherence. Type of treatment centre, nurse availability, and physician time spent with patients at diagnosis also influenced adherence.

P2448

Abstract cancelled

P2449

CLINICAL STUDY OF EARLY ONSET MULTIPLE SCLEROSIS IN ISFAHAN, IRAN

M. Etemadifar1, A.H. Maghzi1
1Medical School, Department of Neurology, Isfahan University of Medical Sciences, Isfahan, Iran

Background and aims: Although Multiple Sclerosis (MS) is considered as a demyelinating disease of young adults, nearly 3% of patients manifest it under the age of 16. The aim of this survey was
to highlight the clinical and demographical features of Early Onset MS (EOMS) in Isfahan and to compare our results with other studies in different regions of the world.

**Methods:** This prospective study concerned MS patients in whom MS started below the age of 16 and have been referred by neurologists and neuropediatricians to the only clinic of MS in Isfahan from October 1997 to February 2003. All EOMS patients underwent MRI and the MRI findings were analyzed according to Barkhof’s criteria. All EOMS patients were followed up for an average of 4.7 years.

**Results:** Among 1238 MS patients, 82 EOMS patients were identified (6.62%). The female/male ratio was 4.47:1. The average age of onset was 14.12 years (ranging from 5 to 16). In 64.63% the onset was monosymptomatic and in the remaining 35.37%, it was polysymptomatic. In EOMS patients 78.05% presented a relapsing-remitting course, 17.07% a secondary-progressive and 4.88% a primary-progressive course. In the last evaluation EDSS score was six or more in only 9.75%. According to Barkhof’s criteria, characteristic MRI findings were observed in 97.56%.

**Conclusion:** In our study a high rate of EOMS was observed that may be because of geographical or racial differences. Our study showed that the Barkhof’s clinical criterion which is mostly used in adult patients could be also applied to EOMS cases.

**P2450**

**THE INFLUENCE OF FUNCTIONAL STATE, DEPRESSION AND FATIGUE ON HEALTH-RELATED QUALITY OF LIFE IN POLISH SUBJECTS WITH MULTIPLE SCLEROSIS**

E. Papuc, H. Bartosik-Psujek, K. Mitosek-Szewczyk, E. Belniak, Z. Stelmasiak

*Department of Neurology, Medical University of Lublin, Poland*

**Aim:** The aim of this study was an assessment of the influence of functional state of Polish subjects with multiple sclerosis on their quality of life, depression and fatigue.

**Methods:** 173 patients with a diagnosis of MS according to McDonald criteria participated in the study (M/F=52/121; mean age: 36.9±8.9; mean disease duration: 8.9±6.6 years; mean EDSS: 4.34±1.84). All subjects were assessed with MMSE, Beck Depression Inventory (BDI), Fatigue Severity Scale (FSS), World Health Organisation Quality of Life Instrument (WHOQOL-100) and with EDSS.

**Results:** Higher level of disability measured in EDSS correlated with worse overall quality of life and worse quality of life in the physical and psychological health domains, worse social relations, lower level of satisfaction with the surrounding environment. Correlations between disability in each functional system separately and quality of life, depression and fatigue were also found.

**Conclusions:**
1. Functional disability, and especially pyramidal and cerebellar dysfunction, bowel and bladder dysfunction, gait impairment are correlated with worse quality of life.
2. Disability in visual system is correlated with limitations in level of independence and impairment of social relations of MS patients.
3. Disability in brain stem functional system and cerebral functional system are correlated with significant limitations of independence level in multiple sclerosis patients.
4. Disability in pyramidal, cerebellar, bowel and bladder functional systems and gait impairment are correlated with worse quality of life in physical and environmental domains and in worse social relations of multiple sclerosis patients.
Comments: So far 14 patients have been reported with post-MTX acute leukaemia. Our 2 patients have similar characteristics: short latency after MTX treatment, acute onset and cytogenetic changes similar to de novo leukaemia. Most of these patients responded to the leukaemia treatment in contrast to leukaemia associated with alkylating substances.

P2453

IVIG TREATMENT IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS: NEW INSIGHTS INTO GENE EXPRESSION PROFILES OF PERIPHERAL T-CELLS
N. Pigard1, H. Kuusisto2, I. Elovaa2, P. Raija2, H-P. Schwarz3, B. Reipert1,2
1BMT-Research LLC, Vienna, Austria, 2Neuroimmunology Unit, Department of Neurology, Medical School, University of Tampere and Tampere University Hospital, Tampere, Finland, 3Baxter BioScience, Vienna, Austria

Intravenous immunoglobulins (IVIG) are used successfully in the treatment of several autoimmune diseases of the central nervous system including multiple sclerosis (MS). Although IVIG seems to have a substantial effect on treatment potential, the underlying mechanisms of action are not fully elucidated, although the beneficial effects of IVIG treatment might be caused by a modulation of the T-cell immune response. The aim of our work was the identification and characterization of genes, involved in the immunomodulatory activity of IVIG in the treatment of exacerbations in relapsing-remitting MS (RRMS). Using microarray we investigated the expression profiles of T-cell fractions of peripheral blood mononuclear cells isolated from 10 RRMS patients treated with IVIG as well as five control patients treated with intravenous methylprednisolone (IVMP). Data were analyzed, using a parametric t-test (Welch t-test). The expression of representative immune-relevant genes was confirmed by Real Time PCR. Among the 33,000 genes examined, we found 360 genes which were at least two-fold differentially regulated. Most of these genes are known to be involved in immune responses, inflammatory responses, proliferation, cell cycle, signal transduction or regulation of transcription. The proteins encoded by differentially regulated genes are likely to be associated with the regulation of disease activity in RRMS-patients. Therefore, we believe that we have identified a set of genes that might be associated with the clinical efficacy of IVIG in patients with RRMS. These genes could serve as diagnostic markers. Furthermore, some of the proteins encoded might provide new targets for drug development.

P2454

WHOLE BLOOD IN-VIVO – IN-VITRO MONITORING OF BIOLOGICAL RESPONSE TO INTERFERON BETA THERAPY IN MULTIPLE SCLEROSIS
M. Vokaer1,2, F. Villez1, A. Ocman1, M. Goldman2, P. Stordeur3
1Department of Neurology, 2Department of Immunology, Erasme Hospital, Brussels, 3Institute for Medical Immunology, Gosselies, Belgium

Background: Interferon beta (IFNb) has shown to be of benefit for the treatment of multiple sclerosis (MS). Some patients may develop neutralizing antibodies (NAB) upon chronic administration of all IFNb products. Neutralizing antibodies are subset of binding antibodies that prevent IFNb from activating its receptor, thereby blocking the biological effects and reducing the clinical efficacy. MxA is an antiviral protein induced by type I interferons and some viruses. MxA gene expression is one of the most appropriate markers for measuring the biological activity of exogenous IFN and is reduced by the presence of NAB.

Patients and methods: RT-PCR method was used to quantify MxA mRNA in whole blood of 17 IFNb-treated patients with CDMS (4 Betaferon, 10 Avonex, 3 Rebif 44 μg). MxA mRNA levels were quantified by RT-qPCR on whole blood in-vivo before and 4 hours after IFNb injection and in-vitro before and 4 hours after whole blood stimulation by 100U/ml of IFNb. Stimulation index was defined as MxA mRNA levels ratio (after injection or stimulation/before injection or stimulation).

Results: An excellent correlation ($r^2=0.92$ $p<0.05$) was found between in-vivo and in-vitro stimulation index. There was also an excellent correlation between the biological results and the clinical responsiveness to therapy.

Conclusions: Whole blood RT-PCR quantification of MxA mRNA revealed a reliable method to monitor the biological response to type 1 IFN in MS. The excellent correlation found between in-vivo and in-vitro stimulation index should allow us to lighten the procedure and thus increase patients’ comfort.

P2455

INTERLEUKIN 2 (-384) GENE POLYMORPHISM IN GREEK PATIENTS WITH MULTIPLE SCLEROSIS
K. Aggelakis1, F. Zacharakis2, P. Kolia1, M. Gkaraveli1, V. Tsimourtou2, E. Dardiotis2, M. Dardioti2, G. Xiromerisiou2, A. Papadimitriou1, G. Hadjigeorgiou1
1Department of Neurology, Department of Ophthalmology, 2Department of Molecular Biology, 3Department of Psychiatry, University Hospital of Larissa, School of Medicine, Larissa, Greece

Background: Multiple sclerosis (MS) results from an interplay between yet unidentified environmental factors and susceptibility genes. Interleukin-2 (IL-2) is a crucial immunoregulatory cytokine with both pro-inflammatory and anti-inflammatory actions, promoting T-cell proliferation during all mediated responses.

Methods: Using standard methods (PCR/RFLP), we analyzed DNA from 223 consecutive Greek patients (148 women and 75 men) with clinically definite MS and from 240 age- and sex-matched controls, in order to study possible association of IL-2 (-384) polymorphism with MS. 123 patients with relapsing remitting and 70 patients with secondary progressive MS were classified as bout-onset (BO) ($n=193, 129$ women), whilst 30 patients (17 women) referred progressive-onset (PO). The age-at-onset was $32.12\pm9.51$ (mean±SD) years for the patients with BO and $32.09\pm9.45$ years for the patients with PO, whilst the disease duration was $8.41\pm7.3$ years and $8.32\pm7.23$ years respectively. Disability was assessed using the Kurtzke expanded disability status scale (EDSS) and was graded as mild (0–3.5), moderate (4–5.5) and severe (6–10). The EDSS score was $3.98\pm2.07$ for patients with BO and $3.99\pm2.07$ for patients with PO.

Results: The population was in H-W equilibrium. Distribution of IL-2 (-384) genotypes and alleles was similar in patients (including all subgroups) and controls.

Conclusion: Our finding suggests that there is no association of IL-2 (-384) polymorphism and disease susceptibility, or type of the disease, age at onset, duration, sex and severity in Greek patients.

P2456

COURSE AND PROGNOSIS IN EARLY-ONSET MULTIPLE SCLEROSIS. A COMPARISON WITH ADULT-ONSET FORMS
F. Ashtari, V. Vashyannejad
Neurology Ward, Alzahra Hospital, Esfahan Medical and Research University, Esfahan, Iran
Multiple Sclerosis (MS) is a chronic demyelinating disease of the central nervous system. In the present study, we reviewed and compared the clinical and paraclinical features of early onset (EOMS) with adult onset MS (AOMS).

**Methods:** This study was descriptive of that performed in Isfahan MS Clinics from Jan 2003 until Aug 2006.

104 patients with clinical onset under 16 years and 123 of adult age were followed for at least 5 years.

**Results:** The mean age of onset was 27.73 in the AOMS and 14.05 in the EOMS. The female/male ratio in EOMS was 4.47:1 vs. 3.92:1 in AOMS. The more frequent clinical course in both MS groups is Relapsing-Remitting (83.7% of EOMS and 84.6% of AOMS patients). The most common initial symptoms in EOMS was optic neuritis followed by parasthesias, while it is parasthesias, optic neuritis in AOMS patients. There is a significant difference between duration of disease and degree of disability in AOMS. 8.7% of EOMS and 12.2% of AOMS patients had a positive family history, and the difference was not significant between two MS groups (p=0.51). Periventricular plaque in MRI was the most frequent finding in both EOMS and AOMS, (63.3% vs. 73.1% p=0.132). 80.8 percent of the patients in the EOMS group and 84.6 percent of the patient’s in the AOMS group had EDSS of less than 3.5 (p=0.21).

**Conclusion:** According to this study there are no significant differences between EOMS and AOMS, so work up and treatment of patients should be same.

---

**P2457**

**FAMILIAL EFFECTS ON THE CLINICAL COURSE OF MULTIPLE SCLEROSIS IN BASHKORTOSTAN**

K.Z. Bakkhtijarova, R.V. Magzhanov, V.F. Tunik, O.V. Zaplakhova

Bashkir State Medical University, Ufa, Russia

From 710 surveyed patients, there were 33 (4.6%) who had relatives with MS in 20 families. Kaplan-Meier analyses did not show differences in time of achievement EDSS=3 and EDSS=6 in familial and typical cases of MS. Familial factors do not significantly affect eventual disease severity.

**Background:** Familial factors influence susceptibility to multiple sclerosis (MS) but it is unknown whether there are additional effects on the natural history of the disease.

**Method:** We evaluated 20 families with ≥2 first-degree relatives with MS for concordance of age at onset, clinical course, and disease severity and investigated transmission patterns of these clinical features in affected parent-child pairs.

**Results:** The greatest number of patients with MS was 3 in three families where mother, daughter and son were ill, in another one there were mother, son and grand daughter, in the third one – 3 daughters. Transfer of illness is observed both on a vertical (mother-daughter, mother-son), and across (brothers, sisters). Our data do not let solve the problem on type of heredity. The age of the beginning of disease is statistically below in familial cases (p=0.035), women fell ill 5 years earlier, than men (p=0.007). The average of scale EDSS (p=0.62) and speed of disease progressing of did not differ from typical MS (p=0.29). Kaplan-Meier analyses did not show differences in time of achievement EDSS=3 and EDSS=6 in familial and typical cases of MS (p=0.17 and p=0.36).

**Conclusion:** Familial factors do not significantly affect eventual disease severity. The results are relevant for counselling patients and have implications for the design of studies seeking to identify factors that influence the natural history of the disease.

---

**P2458**

**PRECIPITOUS INCONTINENCE IN A WOMAN WITH MS**

S. Balasuriya, S. Wimalaratna

Department of Neurology, Great Western Hospital, Swindon, UK

A 39-year-old female, with a 5-year history of multiple sclerosis, presented with attacks of sudden unexpected incontinence. Attacks started with shaking of limbs, followed by board like stiffness of lower limbs that lasted for 30–60 seconds. Symptoms became gradually worse with increasing frequency and duration of the attacks causing inability to stand or walk. Later she developed episodic shaking of upper limbs without stiffness and total paralysis of lower limbs following stiffness lasting up to 2 hours frequently associated with ‘precipitous incontinence’. Interictal neurological examination showed mild spasticity and weakness of lower limbs consistent with previous MS. MRI of brain showed white matter lesions consistent MS but the spinal cord was normal. She was treated with carbamazepine, Baclofen and steroids without benefit. She started complaining of night sweats, joint pains, increasing fatigability and more ‘shaking attacks’. ESR was 56, rheumatoid factor was positive, CXR, thyroid and liver functions were normal. ANA was negative. 5 of 6 blood cultures grew beta haemolytic streptococci. A diagnosis of bacterial endocarditis was made and she was treated with IV antibiotics followed by aortic valve replacement. All her symptoms resolved completely. We concluded that her initial shakings were rigors, secondary to beta-eremia. Episodic rigidity, paralysis and precipitous incontinence are an extreme example of Uthoff phenomenon causing reversible conduction block associated with rise in body temperature.

---

**P2459**

**EFFECTS OF MEDICATION AND NON-PHARMACOLOGICAL INTERVENTION ON ALERTNESS IN MS-PATIENTS – A PILOT STUDY**

P. Calabrese¹, I.K. Penner²

¹Department of Neuropsychology and Behavioural Neurology, Faculty of Medicine, University of Bochum, Germany, ²Department of Cognitive Psychology and Methodology, Faculty of Psychology, University of Basel, Switzerland

**Introduction:** Cognitive deficits belong to the key symptoms in multiple sclerosis (MS). Among these deficits, disturbances of attention and memory have a strong impact on activities in daily living. The aim of our study was to evaluate possible attention-related training effects in combination with pharmacological treatment in MS-patients over a 3-month-period.

**Methods:** We studied altogether 19 MS-patients (mean age =41.26 yrs; mean EDSS =3.29). During the study period patients received IFN-beta-1a treatment (AVONEX, Rebif or Beneferon). While for 12 patients pharmacological treatment started at the beginning of the study, 7 subjects were already on medication. The latter received an attention training over 4 weeks. All patients were investigated on tonic and phasic alertness by a computerized paradigm. The alertness performance was evaluated at baseline and again after 12 weeks. Patients receiving attentional training underwent an intermediate assessment after 4 weeks.

**Results:** IFN-beta-1a treatment had a significant effect on phasic alertness after three months, while tonic alertness was not affected. Convergent to these findings, attention training only influenced phasic alertness.

**Discussion:** Our preliminary results show that IFN-beta-1a treatment has a favourable effect on phasic alertness and on attentional control. As the already medicated patients showed a weaker treat-
Clinical signs of peripheral neuropathy were established in the pathological process based on clinical, electromyographic, and nerve conduction studies. The likelihood of involvement of the peripheral nerves in multiple sclerosis (MS) was the objective of the study. In some cases of peripheral nerve impairment, pathological changes were recorded. Electrophysiological examinations are frequent in MS patients, and due to the fact that some proteins of the peripheral myelin are similar to the myelin proteins of the CNS, the antibodies which react with the CNS myelin partially react with the myelin of the PNS.

P2460
EVALUATION OF THE 2005 MCDONALD MRI CRITERIA FOR DISSEMINATION IN SPACE IN AFRO-CARIBBEAN PATIENTS WITH CLINICALLY ISOLATED SYNDROMES

N. Chausson, S. Olindo, A. Signate, J. Joux, D. Smadja, P. Cabre
Department of Neurology, CHU Fort-France, Martinique

In 2005, McDonald MRI criteria for dissemination in space have been revised to improve diagnosis of MS in non-Caucasians. The aim of this work is to assess their performance in the Afro-Caribbean population. We included patients with a first clinically isolated syndrome (CIS). Baseline brain and spine (95% of the patients) MRI examination were available within 3 months after onset of CIS. The development of a second clinical event was used as the main outcome indicating clinically definite multiple sclerosis. 79 patients (66F/13M) were included between 1998 and 2006 (mean age 36, range: 12–82; mean follow-up 38 months, range: 3–108). CIS was classified: spinal cord (37%), optic neuritis (28%), brainstem (22%), multiregional (9%), hemispheric (4%), and undetermined (1%). Overall conversion rate was 53% (mean delay: 15.7 months). The McDonald criteria revised for dissemination in space were fulfilled in 31.7% (Sensitivity =31% (±14%); specificity =68% (±15%); PPV=52%, NPV =46%). We isolated a subgroup of 41 patients without relapsing neuro-myelitis optica for whom follow-up exceeded 2 years. (Sensitivity =40% (±17.5%); specificity =55% (±29%); PPV=71%, NPV =25%). The Afro-Caribbean population is characterised by a strong proportion of CIS in the spinal cord. This may explain low sensitivity of 2005 McDonald Criteria for dissemination in space. Further prospective studies emphasizing MRI spinal cord features are needed to improve diagnostic criteria in population of African descent.

P2461
IMPAIRMENT OF PERIPHERAL NERVES IN MULTIPLE SCLEROSIS

V. Lisiuc1, D. Gherman1, M. Gavriliuc2, T. Crani2, S. Plesca2, O. Odanic3, O. Micev
1Department of Neurology, Medical State and Pharmaceutical University, 2Institute of Neurology and Neurosurgery, Chisinau, Moldova

Signs of peripheral nerves impairment at clinical, electrophysiological, and morphological levels are recorded in some cases of multiple sclerosis (MS). The objective of the study was to establish a pattern of clinical and subclinical impairment of the peripheral nerves in MS.

Methods: The likelihood of involvement of the peripheral nerves in the pathological process based on clinical, electromyographic and nerve conduction studies was analyzed in a group of 30 consecutive patients with definite MS (21 females and 9 males aged between 15 and 49 years old, average age 33.57±1.53 years).

Results: Clinical signs of peripheral neuropathy were established only in 2 cases. They were manifested by distal distribution of sensory loss in „stocks and gloves“ presentation, absence of ankle reflexes. However the electrophysiological examination revealed pathological changes in 16 patients (53.3% cases). The performed study established the existence of subclinical changes specific for a neuropathy in MS cases. These modifications could be detected by means of electrophysiological examination and consist in increasing of the distal latency, diminishing of the nerve conduction velocity in motor and sensory fibres of the peripheral nerves, prolongation of F waves latency.

Conclusions: Signs of impairment of the peripheral nerves based on electrophysiological examinations are found frequently in MS patients. Due to the fact that some proteins of the peripheral myelin are similar to the myelin proteins of the CNS, the antibodies which react with the CNS myelin partially react as well with the myelin of the PNS.

P2462
SMOKING HABITS IN PREGNANT MS WOMEN

J. Dahl1, K.M. Myhr1, A.K. Dalveit2, R. Skjerven2, N.E. Gilhus1
1Section of Neurology, Department of Clinical Medicine, University of Bergen and Department of Neurology, Haukeland University Hospital, 2Section for Epidemiology and Medical Statistics, Department of Public Health and Primary Health Care, Medical Birth Registry of Norway, University of Bergen, Norway

Multiple sclerosis (MS) in pregnant women leads to increased risk for reduced birth weight, compared to non-MS births. To evaluate risk factors for the lower birth weight of the neonates among MS women, we investigated smoking habits and social factors in pregnant MS women versus controls in the Medical Birth Registry of Norway. A total of 372,128 births were registered from December 1st, 1998 until October 6th 2005, and 250 of them by MS mothers. Smoking during pregnancy was not increased in the MS group. Smoking affected birth weight similarly in both the MS and the control groups. The MS group had a larger reduction in smoking rate during pregnancy than the control group during the studied years. The daily amount of cigarettes among smokers during pregnancy was lower in the MS group (mean 5.7±4.1) compared to the controls (7.4±4.6) (P=0.07). More MS women stopped smoking during pregnancy compared to the controls (34.1% versus 25.6%). Higher education (≥13 years) was more frequent in the MS group (54.0%) compared to the controls (41.1%) (P=0.06, OR 1.28, 95% CI 0.99-1.66, adjusted for maternal age). The smoking MS group showed no increase in birth complications, operative interventions or negative birth outcome, compared to the smoking controls.

Conclusions: No interaction between MS and smoking that influenced birth weight was detected. Smoking during pregnancy cannot explain the reported birth weight reduction found among MS mothers.

P2463
LATE ONSET METACHROMATIC LEUKODYSTROPHY MIMICKING THE DIAGNOSIS OF MULTIPLE SCLEROSIS

S. Chebel, M. Ammar, A. Boughammoura, M. Frib-Aved

Department of Neurology, University Hospital of Monastir, Tunisia

Background: Metachromatic leukodystrophy (MLD) is an inherited, metabolic, degenerative disease of the nervous system. It is caused by a deficiency of a lysosomal enzyme-arlsophatase A, with the storage of cerebroside sulphate and demyelination affecting mainly the central and peripheral nervous system.

Objective: We present a case of metachromatic leukodystrophy (MLD) of the adult onset type, in which atypical initial course and neuroimaging could suggest multiple sclerosis.

Case report: It is a 42-year-old woman. The clinical onset of the disease was at the age 18. The first neurological symptoms included depressive syndrome, associated later to progressive cognitive...
deterioration and pyramidal syndrome without peripheral nervous system involvement. T2 and FLAIR weighted MRI showed high intensity areas in the white matter, mainly periventricular. Biological essays including screening essay of arylsulphatase A activity confirmed the diagnosis of late onset MLD. Molecular genetic examination of a DNA sample obtained from the patient is current.

**Comments and conclusion:** The clinical symptoms and neuro-imaging in our patient could suggest a cognitive form of multiple sclerosis (of the primary progressive type). We recommend that the diagnosis of MLD must be considered in all young adults with multiple sclerosis like white matter T2 lesions.

**P2464**

**ALTERATION OF VISUAL ATTENTION IN PATIENTS WITH MULTIPLE SCLEROSIS**

Sz. Gulyas, V. Zyer, Zs. Farkas, A. Kamondi, I. Szirmai

Department of Neurology, Semmelweis University, Budapest, Hungary

Multiple sclerosis (MS) is a widespread neurological disease affecting mainly the periventricular white matter due to demyelinated plaques. These plaques may interrupt the connection of frontal and parietal association areas which play an important role in visual attention functions. The optokinetic nystagmus (OKN) is a reflexive, periodic eye movement which helps to hold the image of a moving target on the fovea. Visual attention is needed to maintain continuous OKN, therefore OKN might be used to examine visual attention. 30 patients with MS (periventricular or diffuse type in remission) and 18 age- and gender-matched controls were examined. OKN was stimulated by computerized rotating drum projected onto a screen, stripes were moving to the right and left with 30 degrees velocity. Eye movement was recorded by standard electro-oculographic techniques. We measured the latency of OKN, the maximum duration of continuously appearing OKN epochs, the average duration of each continuous OKN period. Relative duration of OKN was calculated as the ratio of the total duration of OKN and the total duration of stimulation. Irrespective of the direction of the stimulation the maximum duration decreased to one third of control value, the average duration of OKN epochs decreased by 13 seconds, as well as the relative duration of OKN decreased by 30% in MS patients. These changes were statistically significant. The latency of OKN was similar to that of the control group. Our results suggest that MS may cause a disconnection syndrome affecting the fronto-parietal network responsible for visual attention.

**P2465**

**CEREBRAL VENOUS THROMBOSIS IN A PATIENT WITH CLINICALLY ISOLATED SYNDROME, SUGGESTIVE OF MULTIPLE SCLEROSIS ONSET AND REVIEW OF LITERATURE**

M.H. Harirchian, A. Baiati

Iranian Center of Neurological Research, Imam Khomeini Hospital, Tehran University of Medical Science, Tehran, Iran

**Background:** Cerebral venous thrombosis (CVT) may occur at any age and may be idiopathic or secondary to various causes. It has been described in patients with multiple sclerosis (MS). We report a case with symptoms and signs of inflammatory demyelinating disease as a clinically isolated syndrome (CIS) suggestive of MS onset, who developed CVT after lumbar puncture and during high dose of methylprednisolone pulse therapy.

**Case report:** Our patient, a 43-year-old woman, was admitted to our department with right blurred vision and gait ataxia. She had no history of cardiovascular events or risk factors. Brain MRI showed hypersignal plaques in the white matter which were suggestive of a demyelinating disease. The venous sinuses were patent. Routine investigations for vasculitis were negative. A lumbar puncture was performed and cerebrospinal fluid (CSF) was within normal limits. She received high-dose methylprednisolone (1 g/day) for 5 days. 5 days later she developed continuous headache and hemiparesis and seizures and repeated brain MRI and MRV showed superior sagittal sinus thrombosis. Routine blood and hypercoagulative work-up were normal.

**Discussion:** It seems that high dose corticosteroid therapy after lumbar puncture may be a risk factor for CVT specially when associated with other predisposing risk factors and CVT must always be suspected when postural post-LP headache evolves into a severe continuous headache specially when there was a sequence of LP followed by high dose corticosteroid treatment.

**P2466**

**FAVOURABLE CLINICAL AND MRI EVOLUTION OF A PATIENT WITH MULTIPLE SCLEROSIS AND COELIAC DISEASE, TREATED WITH A GLUTEN-FREE DIET**

C. Hernandez-Lahoz1, L. Rodrigo1, S. Rodriguez2, E. Santamarta1, C. Lopez-Larrea1

1Departments of Neurology; 2Department of Gastroenterology.

**Department of Radiology; 3Department of Immunology, Hospital Universitario Central De Asturias, Oviedo, Spain**

We have followed the prolonged and favourable evolution of a patient with Multiple Sclerosis (MS) and Coeliac Disease (CD), treated with a gluten-free diet (GFD). In 1999, after the delivery of her second child, a 37-year-old woman noticed numbness in the left part of her body, which resolved without treatment. A year later, she presented paresthesias on the other side and dermatitis herpetiformis. In 2001, she suffered neck and interscapular pain and mild numbness and weakness of the legs. She was admitted to hospital with a diagnosis of myelitis. MRI scan showed multiple spinal cord and brain lesions, which were diagnosed as RRMS. A course of intravenous methylprednisolone was given and she gradually improved. Later, she began treatment with subcutaneous IFN-1a, 44 mcg/3 times weekly. In 2002, she presented an acute episode of abdominal pain, diarrhoea and loss of weight and was hospitalized. IgA anti-tissue transglutaminase antibodies (TTG IgA) were 186.6 U/ml. HLA-DQ2 was positive. The intestinal biopsy showed stage 3b of Marsh. The patient was diagnosed as having CD and put on a GFD, which has been followed strictly until now. She recovered weight and is completely asymptomatic (EDSS=0). TTG recovered normal values in the first year. Duodenal biopsies repeated after 2 years showed normal mucosa, without atrophy or inflammation. IFN-1a was reduced to 22 mcg and finally stopped in 2006, without relapses. MRI scan confirmed reduction of lesions without gadolinium enhancement. In this case, we suppose some ethiopathogenic relationship exists between the 2 immunomediated disorders.

**P2467**

**VESTIBULAR AND COORDINATING DISORDERS IN MULTIPLE SCLEROSIS PATIENTS**

Y. Holets, S. Likhachev, A. Kachinsky

Republican Research Center of Neurology and Neurosurgery, Minsk, Belarus

**Background:** Balance disorders are common in multiple sclerosis (MS) patients.
Purpose: To investigate structure and severity of vestibular and coordinating disorders in MS patients.

Methods: 92 MS patients – main group (49 women, 43 men; mean age 42.5±10.16, EDSS 3.75±1.26) and a control group of 53 healthy persons were examined by vestibulometry (VM) and dynamic posturography (DP). VM was performed using the method of electronystagmography. Horizontal and vertical vestibulococular reflexes (HVOR and VVOR), VOR suppression reaction by stare fixation during active sinusoidal head rotation were studied. Gain VOR was estimated. Postural function was assessed with open eyes in two regimens of biofeedback: visual and acoustic (VBFB and ABFB) using the computer platform for DP. Effectiveness patient movements (EPM), mean postural response time (MPRT) and coefficient of visual participation (CVP), which characterized system relations between sensory functions and movement, were estimated.

Results: Mean gain VOR in main (control) group was 1.1±0.09 (0.4±0.04), VOR suppression – 0.55±0.05 (0.05±0.01). HVOR and VVOR were suffering, wasn’t found any significant difference between them.

Mean results of DP in main (control) group were: during VBFB – EPM 44.0±14.2 (68.3±15.9)%, MPRT 0.63±0.12 (0.47±0.12) sec.; during ABFB – EPM 54.9±7.4 (66.7±16.9)%., MPRT 0.51±0.11 (0.429±0.12) sec.; CVP: –10.89 (–46.67). 

Conclusion: Founder high gain VOR, significant changes in stare HVOR and VVOR suppression, low CVP during DP are evidence of considerable disconnection between main integrators of nervous system and pathological clinical response during vestibular stimulation in MS patients.

P2469

A CASE OF SEVERE LEFT VENTRICULAR DYSFUNCTION IN A YOUNG FEMALE WITH MULTIPLE SCLEROSIS

P. Inverizzo1, F. Rossi1, M. Turri1, M. Toniolo1, G. Morando1, C. Vassanelli2, N. Rizzuto1, M.D. Benedetti1 1Department of Neurological and Visual Sciences, Section of Neurological Clinic, 2Department of Biomedical and Surgical Sciences, Section of Cardiology, University of Study in Verona, Italy

Heart dysfunction is an unusual event in patients with Multiple Sclerosis (MS). Mitoxantrone-induced cardiotoxicity is well recognized, but some cases with MS and cardiac involvement have been recently described also in patients not treated with this therapy. We describe the case of a 36-year-old woman with MS diagnosed at 27, a family history of MS (a brother), and treated with azathioprine for 1 year, who came to the emergency department for severe asthenia which started the night before. Her last SM relapse happened about 1 year before and last EDSS score was 2.5. She had stuporous, hypothermic (32.8°C), hypotensive (80/60 mmHg) and tachycardic (120 bpm rhythmic). An echocardiography showed left ventricular failure with ejection fraction of 10%. She was admitted to the Intensive Care Unit and treated with inotropic therapy. Hematochemical exams showed an aspecific inflammatory status and cardiac damage indexes. Coronary angiography was normal. A myocardial biopsy was not diagnostic. In the hypothesis of an inflammatory pathogenesis a treatment with Immunoglobulin was started (2 g/Kg i.v. for 5 days).

After 2 days of treatment she recovered completely. A cardiac MRI did not show signs of inflammation. Even without pathological or imaging support, a myocarditis was the most likely cause of cardiac dysfunction with complete regression in a few days in this young woman. Myocarditis secondary to viral infections, in fact, has an autoimmune pathogenesis and a significant comorbidity between MS and other autoimmune diseases is recognized. Possible etiologic mechanisms and case reports in the literature are discussed.

P2470

CLINICAL AND DEMOGRAPHIC FEATURES OF MULTIPLE SCLEROSIS IN AN ITALIAN REGISTER: A CROSS-SECTIONAL, ECOLOGIC STUDY

C. Pecori, C. Lucchesi, V. Pellicia, D. Benvenuti, P. Riani, C. Frittelli, P. Maritato, F. Manfredonia, L. Pasquali, G. Meucci, A. Indice, L. Murri 1Department of Neurosciences, University of Pisa, Italy

Object: Multiple sclerosis (MS) is a chronic demyelinating disease of the nervous system, with variable clinical presentation and course. Epidemiological patterns widely differ and account for a high prevalence and incidence in some geographic areas.

Method: We have analysed the register of patients referred to our clinic for demyelinating disorders at University of Pisa from 1987 to date.

Results: Over 10 years, a total of 917 patients were referred to the centre, 856 of whom had MS. In accordance with their clinical course, 73.3% patients were diagnosed as Relapsing-Remitting MS (RRMS), 11.3% as Secondary Progressive (SPMS), 5.3% as Primary Progressive (PPMS), while 10.1% of cases were Clinically Isolated Syndromes (CIS). Female/male ratio was 1.79. Mean age at disease onset was 33.5 (range 12–67) years, and mean age at diagnosis (McDonald criteria) was 37.01 (range 12–71). MS onset averaged 32.47 years in RRMS (range 12–67), 43.71 in PPMS (range 17–58), 34.95 in SPMS (range 13–57), and 32.58 in cases of...
CIS (range 16–56). Progression toward SPMS took 11.18 years on average (range 2–35) after disease appearance, with patients mean age of 43.76 years (range 30–63).

Conclusion: Results are consistent with previous observations from epidemiological studies in the country as far as clinical and demographic MS features are concerned. [Study supported by an unrestricted grant from the Tuscany Regional Health Service]

P2471
PARAOXONASE (PON) 1 ACTIVITY IN MULTIPLE SCLEROSIS PATIENTS
A. Jamroz-Wisniowska1,2, H. Bartosik-Psujek1, J. Beltowski1, Z. Stelmasiak1
1Department of Neurology, 2Department of Pathophysiology, Medical University, Lublin, Poland

Background: Multiple sclerosis (MS) is the most common demyelinating disease of the central nervous system of unknown etiology. The possible role of oxidative stress in the pathogenesis of MS is taken into consideration. Paraoxonase (PON) 1, an esterase associated in blood with high-density lipoproteins (HDL), plays a role in the antioxidant properties of HDL. PON1 activity was found to be lower in several autoimmunological diseases. The aim of this study was to evaluate plasma PON1 activity in patients with MS.

Methods: 117 MS patients and 129 healthy individuals matched for age participated in the study. The MS group comprised 38 men and 79 women; mean age was 37±9.41 years (range 19–55). Depending on disease course, MS patients were divided into relapsing-remitting (n=58) and progressive groups (n=59). Plasma PON1 activity toward synthetic substrates and lipid profile were examined.

Results: We found significantly higher PON1 activity in MS patients compared to control group. There was also higher concentration of cholesterol and triglycerides in MS group. No statistically significant differences between MS subgroups were found.

Conclusions: PON1 activity was higher in MS patients, similarly as total cholesterol, HDL and LDL cholesterol and triglycerides concentration. Table. Results.

<table>
<thead>
<tr>
<th>PON1 activity [IU/L]</th>
<th>MS patients</th>
<th>Control group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>toward paraoxon</td>
<td>176±279.56</td>
<td>136±139.44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>toward phenyl acetate</td>
<td>127±82.52</td>
<td>75±47.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>toward paraoxon in 1M NaCl buffer</td>
<td>416±1743.34</td>
<td>607±4723.52</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P2472
ANTIPHOSPHOLIPID SYNDROME MIMICKING MULTIPLE SCLEROSIS (APS-MS) AND MULTIPLE SCLEROSIS (MS)
L.A. Kalashnikova1, B.D. Dzhumantaeva1, E.N. Alexandrova1, A.A. Novikov1, A.V. Peresedova1, M.V. Krotenkova1, O.S. Korepina1
1Institute of Neurology, 1Institute of Rheumatology, Moscow, Russia

APS sometimes may mimic MS. The aim – to compare clinical and laboratory features of APS-MS and MS.

Material and methods: 16 patients with APS-MS and 30 patients with MS were studied. All patients underwent clinical, MRT, aPL study (anticardiolipin antibodies – aCL, lupus anticoagulant – LA), visual evoked potentials (VEP).

Results: Clinical manifestations were characterized by remittent neurological symptoms. APS-MS patients more often developed hemiparesis (63%) than MS-patients (7%, p<0.05), while the latter more often developed low paraparesis and vestibulocerebellar symptoms (correspondingly, 50% and 93% vs. 6% and 44% in APS-MS, p<0.05). MS patients were more disabled than APS-MS patients (correspondingly, 3.0±1.02 and 1.0±0.24, Kurtzke scale, p<0.05). All APS-MS patients had systemic and neurological APS manifestations (thrombosis, miscarriage, thrombocytopenia, anaemia, epilepsy, chorea in their past history), while these occurred very rarely in MS (3%, p<0.05). APL of moderate or high positivity were found in APS-MS (aCL – 75%, LA – 69%) and correspondingly in 14% and 23% of MS (weak positivity) (p<0.05). MPT revealed multiple lesions in white hemispheric matter in MS as well as APS-MS patients. VEP showed pathological changes in 58% APS-MS and 64% MS patients (p<0.05).

Conclusion: Differential diagnosis between APS-MS and MS is based on the presence of typical clinical and immunological markers of APS in APS-MS patients and some peculiarities of local neurological symptoms. MRT and VEP do not help to differentiate these independent entities.

P2473
MULTIPLE SCLEROSIS TREATMENT IN GREECE: COST AND BENEFIT
E.E. Karageorgiou1, S. Sotiri1, C. Giannoulis1, M. Polyzoi1, P. Tarla2, N. Logiotatos2, H. Papageorgiou1, C.E. Karageorgiou1
1Department of Neuroscience, University of Minnesota, Minneapolis, MN, USA, 2Neurology Department, Athens General Hospital, Athens, Greece

Objective: The purpose of this study was to determine the cost of managing Multiple Sclerosis (MS) in Greece and to investigate its impact on the quality of life and the progression of the disease.

Patients and methods: A questionnaire was given to all patients with Clinical Definite MS according to the McDonald Criteria who visited the MS Center of Athens General Hospital “G. Gennimatas” over a period of 6 months. The information acquired, reflected the progress and current state of the disease, the disease associated cost for the patient and the National Health System and an assessment of the quality of life according to the EuroQoL. The costs represented direct and indirect costs (e.g. medical care, laboratory examinations MRI, evoked potentials, care giver cost, benefits).

Results: Patients included were men and women with a mean age of 40 years and mean disease duration of 8 years. A major percentage of the cost for the patient was the indirect cost, increasing the burden of the disease.

Conclusions: The National Health System may deal mostly with direct cost, but dealing with indirect cost is equally important for the patient. This effort has started with “help at home” programs which are still in the beginning and need more organization and financial help.

P2474
HETEROGENEITY OF FATIGUE IN MULTIPLE SCLEROSIS
D.S. Kasatkina, N.N. Spirin
Department of Neurology, Yaroslavl State Medical Academy, Yaroslavl, Russia

Background and objectives: The pathophysiology of fatigue in MS is not known. In recent years, there has arised a point of view that fatigue is a complex syndrome, and we have tried to divide it to some parts in accordance with the clinic.

Methods: 46 MS patients (aged 18–49 years) with the duration of the disease 1.0–9.6 years and EDSS score 1.5–4.0 were enrolled in the study. All individuals completed Malkova’s Asthenia Scale
Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) of autoimmune origin and is the most common disabling neurologic disease in young adults. Axonal loss and demyelination occurs in MS. To evaluate brain atrophy, sophisticated methods, not widely applied in clinical practice, are used. The influence of MRI linear parameters and focal MRI changes on clinical disability are not widely described.

Objective: To determine the relation between focal changes in MRI, measurements of brain atrophy and general disability in MS patients and to select linear MRI parameters mostly specific to MS atrophic processes.

Methods and results: 50 MS patients (58% female and 42% male) with mean age of 37.92±1.45 years (yr) and disease duration of 11.8±9.17 years with brain MRI were evaluated. Linear MRI parameters to measure local atrophy were applied. Estimation of disability was performed by using Expanded Disability Status Scale [EDSS] and was stated to be 3.17±1.84. Width of third ventricle, bicaudatus index, bifrontal index, Husmann index, index of frontal atrophy, Evans index and index of corpus callosum were measured to evaluate brain atrophy.

Conclusion: Disability of MS patient is not influenced by demyelinated lesion load but is reflected by parameters describing brain atrophy. Width of third ventricle and bicaudatus index are sensitive markers revealing brain atrophy and could be used to measure progression of brain atrophy in MRI describing MS disability.

Background: Several lines of evidence suggest that multiple sclerosis (MS) and the sleep disorder narcolepsy might overlap in symptoms and pathophysiology. Both disorders are associated with the same specific HLA-types. Case reports of co-existent narcolepsy and MS are known, and excessive daytime sleepiness – the main symptom of narcolepsy – is reported by the majority in some MS populations. Narcolepsy patients lack the sleep-wake-regulating neuropeptide, hypocretin-1, in the hypothalamus and in the cerebrospinal fluid (CSF Hypocretin-1). It is unclear whether the hypocretin-system is intact in MS, as case reports show undetectable CSF hypocretin-1 levels during MS attacks of hypersomnia, while normal levels are found in small studies of MS in remission.

Aims and methods: We systematically investigated levels of excessive daytime sleepiness (by the Epworth sleepiness scale (ESS)) and CSF Hypocretin-1 in 48 consecutive patients with relapsing-remitting MS (RRMS) or monosymptomatic optic neuritis (ON). We also evaluated whether ESS and CSF Hypocretin-1 levels fluctuated during attack and remission.

Results: 25 patients were in attack and 23 in remission. ESS was normal during attacks (5.7±3.0) and remission (5.3±2.7) with no statistically significant difference between the groups (p=0.74). CSF-hypocretin-1 levels were normal (455.93±40.59 pg/ml) and no statistically significant difference between the groups (p=0.50). A performed MRI scan revealed no hypothalamic lesions.

Conclusion: Our results suggest that RRMS and ON are generally associated with normal levels of daytime sleepiness levels and functional hypocretin-neurons. Moreover, the clinical fluctuation of RRMS and ON is not associated with fluctuation in daytime sleepiness or CSF hypocretin-1.
Results: Fatigue was present in 29 MS patients (66%) and in 8 controls (26.7%) (p=0.0002). Anxiety was noticed in 11 MS patients (25%) and in 2 controls (6.7%) (p=0.002). Depression was diagnosed in 3 MS patients (6.8%) and in 2 controls (6.7%) (p=0.13). Frequency of fatigue was similar in women and men (67.7 vs. 61.5%), but anxiety and depression were more common in women (A: 32.3% vs. 7.7%; D: 0% vs. 9.7%). There was no correlation between fatigue and EDSS, age and duration of the disease. An association between fatigue and depression, but not anxiety, was observed.

Conclusion: Fatigue is a very common symptom in MS, sometimes associated with depression. It can be easily diagnosed by usage of FSS and should be considered in every patient with MS, independently from age, sex, disability and duration of the disease.

P2479
INTERHEMISPHERIC INHIBITION IN PATIENTS WITH VERY EARLY RRMS
Department of Neurology, JW Goethe-University, Frankfurt am Main, Germany

Objective: The corpus callosum (CC) is often and early affected in relapsing-remitting multiple sclerosis (RRMS). We sought to study the integrity of the motor CC by paired transcranial magnetic stimulation (TMS) in a well defined sample of early RRMS patients.

Methods: 13 patients with early RRMS (age 32±6 years, EDSS 1.3±0.65, disease duration, 17±15 months) and 12 healthy controls (age 31±9) participated. Paired TMS was used to study interhemispheric inhibition at one short (12ms, SIHI) and one long interstimulus interval (40ms, LIHI) according to an established protocol (Ferbert et al. 1992). Conditioning pulse (S1) intensities varied from 100%-150% of resting motor threshold.

Results: SIHI was significantly less in RRMS than controls (p=0.04), in particular at high S1 intensities. LIHI was not different between groups but there was a significant interaction between S1 intensity and group (p=0.0004). This was explained by a higher LIHI threshold in RRMS while both groups reached similar LIHI levels at high S1 intensities.

Discussion: We show for the first time that IHI is deficient in a group of very early RRMS patients. The decreased SIHI is most likely explained by demyelination of the motor CC and hence a reduction of callosal conduction velocity, while the higher threshold but normal maximum level of LIHI suggests that this long-interval interhemispheric inhibition can be fully recruited but is less effective than in healthy controls, possibly also due to chronodispersion. In conclusion, findings suggest that SIHI and LIHI detect demyelination of the motor CC very early in the course of RRMS.

P2480
MATHEMATICAL MODELING OF A MULTIPLE SCLEROSIS TYPE AT THE START OF DISEASE
N.P. Voloshyna, M.I. Tabachnikov, I.L. Levchenko, T.V. Negreba, T.N. Tkachova
Department of Neuroinfections and MS, Institute of Neurology, Psychiatry and Narcology, AMS of Ukraine, Kharkov, Ukraine

Prognostication of multiple sclerosis (MS) type, despite its actuality, is a complicated methodological problem. We made an attempt by means of mathematical modelling using discriminant analysis to predict future MS type at the start of the disease’s clinical manifestations. The clinical indices in 42 patients with MS and 230 MS patients with known type of disease (relapsing-remitting, secondary progressive and primary progressive) were compared. The indexes characterizing MS-onset for every 3 types of disease were transformed into numerical means – classifying functions. The meanings of 3 classifying functions were calculated using special mathematical apparatus; the highest numbers obtained indicated future MS type. The mathematical model check-up on 230 patients with known MS type showed prognosis coincidence in 88% of cases indicating its reliability. The results of mathematical prognosis using obtained model in patients with MS start (main group) were compared with expert physician’s evaluation. Simple expert’s prognosis was received for 28 patients, 25 of them completely coincided with the mathematical prognosis. 14 patients had uncertain expert’s prognosis which indicated two possible MS types (relapsing-remitting or secondary progressive). At the same time mathematical prognosis for these patients coincided with these two possible MS types. The principle divergence in mathematical and expert’s prognosis was only in 3 of 42 patients, and the mathematical prediction error compared with expert’s was low and did not exceed 7%. Discriminant analysis allows a reliable model for future MS type mathematical prognosis using the disease start characteristics to be obtained and could be widely applied in clinical practice.

P2481
PAIN INFLUENCE ON DEPRESSION AND ANXIETY IN PATIENTS WITH MULTIPLE SCLEROSIS
I.V. Marjanovic, J.R. Kostic, T.D. Pekmezovic, J.S. Drulovic
Institute of Neurology, Clinical Centre of Serbia, Belgrade, Serbia

Objective: The aim of the study was to determine possible correlation between pain, anxiety and depression, measured by Hamilton Anxiety Scale (HAS) and Hamilton Depression Rating Scale (HDRS), in patients with multiple sclerosis (MS).

Methods: A group of 32 consecutive patients from outpatient clinic settings from the Institute of Neurology, Belgrade, who met Revised McDonald criteria (2005) for MS were enrolled in this cross-sectional study. We used a structured interview for registration of pain and sensory symptoms (acute and chronic pain syndromes were included), HAS and HDRS. The Spearman’s correlation coefficient was used for data analysis.

Results: A total of 32 MS patients, 7 men and 25 women were included. The mean age at examination was 40.7±9.4 years. The duration of disease was 11.1±6.1 years. The mean EDSS was 4.5±2.2. The course of the disease was relapsing-remitting in 20 (62.5%) patients, secondary progressive in 11 (34.4%) and primary progressive in one (3.1%). On examination 8 (25.0%) patients had acute pain syndrome. Chronic pain was present in 11 (34.4%) cases. Patients with pain reported an average pain intensity of 4.8±1.9 on Visual Analog Scale. More than half of those with pain (59.4%) rated it as moderate, and 25% as severe. We noted significantly positive correlation between chronic pain and HDRS score (p<0.01), and between acute pain and HAS score (p<0.01).

Conclusion: These results suggest the importance of the association of pain with anxiety and depression in MS, implicating the necessity for appropriate treatment of these conditions in MS patients.

P2482
THE ROLE OF AXONOPATHY IN THE DEVELOPMENT OF CENTRAL AND PERIPHERAL DEMYELINATION
D.M. Merkulova1, 2, Y.A. Merkulov1, 2, P.A. Chernova1, 2
1B.M. Gekht Peripheral Nervous System Diseases Diagnostic and Treatment Center, JSC, 2Institute of General Pathology and Pathophysiology, Russian Academy of Medical Science, Moscow, Russia

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
Aim: To estimate the role of axonopathy in the development of the demyelinating processes in the central and peripheral nervous system.

Methods: Thorough clinical, neuroimaging and electrophysiological examination of 43 patients (16 men, 27 women 32.8±7.9 y.o.) with Multiple Sclerosis (MS) and 144 patients (88 men, 56 women 42.2±10.9 y.o.) with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).

Results: The prevalence of MRI hypointensity T1 lesions ("black holes") was established in 28% of cases in MS patients, regional cerebral cortex atrophy – in 46%, significantly associated with the degree of invalidization according to EDSS (Kendall τ=0.38 and 0.43; p=0.038 and 0.021, respectively). The average degree of fatigue according to FSS was 4.9 [3.6; 5.4]. A reliable increase in central conduction time during the exhaustion (p=0.016), along with the absence of the disturbance of reliability in neuromuscular transmission and the absence of the postactivational phenomena, enabled us to assume the predominance of central mechanisms in the formation of the phenomenon of fatigue in MS. At the same time signs of the involvement of the peripheral nervous system were revealed in 34.9% of cases in the group of MS patients, while the presence of CNS activity was noted in the clinical and electrophysiological picture in 12.5% of CIDP patients.

Conclusion: The obtained data expand the existing opinion regarding mechanisms of the formation of axonopathy in CNS, relying on the proofs of the development of the axonal-demyelinating processes in CIDP – the most accessible model of demyelination for the study using contemporary neurophysiological methods.
P2486
FATIGUE AND DEPRESSION IN MULTIPLE SCLEROSIS – CORRELATION WITH QUALITY OF LIFE
S. Miletic Drakulic1, S. CabaKapka2, Z. Knezevic1, N. Todorovic2, G. Toncev2
Department of Neurology, Clinical Centre Kragujevac, Serbia

Background: Fatigue and depression are common features of multiple sclerosis (MS), which could also impact on daily life.

Objectives: To explore fatigue and depression in multiple sclerosis and to determine the relationship between these symptoms and quality of life (QOL).

Methods: The study comprised 60 patients with clinical definite MS: relapsing-remitting MS 46 (76.7%), secondary progressive MS 12 (20%) and primary progressive MS 2 (3.3%). Mean disease duration was 8.1±5.5 years, mean EDSS (Expanded Disability Status Score) was 3.5±1.8 (range 1–8). Fatigue was measured by the Fatigue Severity Scale (FSS). Depression was measured by Beck Depression Inventory (BDI). QOL was assessed using the health–related quality of life questionnaire SF-36.

Results: The global FSS score was 3.9±1.9 (range 1–7) and BDI was 10.8±10.1 (range 0–39). FSS scores significantly correlated positively with BDI scores (r=0.004). The severity of fatigue was significantly correlated with aspects of quality of life (r=−0.743; p<0.000). Particular mental health (r=−0.749; p=0.000). There was significant correlation between the severity of depression and impaired quality of life (r=−0.684; p=0.000).

Conclusions: This study demonstrates that fatigue and depression are associated with impaired QOL in MS.

Key words: multiple sclerosis, fatigue, depression, quality of life

P2487
RASCH ANALYSIS OF THE FATIGUE SEVERITY SCALE IN MULTIPLE SCLEROSIS
R.J. Mills1, R.S. Nicholas1, O. Malik2, C.A. Young1
1Department of Neurology, Walton Centre for Neurology and Neurosurgery, Liverpool, 2Department of Neurology, Charing Cross Hospital, London, UK

Background: The 9-item, fatigue severity scale (FSS) has been widely used as an outcome measure in multiple sclerosis (MS).

Objective: To assess the FSS for the fundamental requirements of measurement i.e., unidimensionality, order and additivity by application of the Rasch measurement model.

Method: The FSS was sent by post to patients with clinically definite MS in two centres in the UK. Analysis was based on 415 records (55% response).

Results: The 9-item scale did not fit the Rasch model. Two items had disordered category thresholds. Items 1 and 2 had the greatest misfit with very high positive fit residuals (each 5.5) indicating a high level of redundancy for the scale. Item difficulties were tightly clustered around an arbitrary mean of zero logits, which is typical of ordinal level scaling. Person-item targeting was reasonable although there was a ceiling effect of 8%. A basic fit could be achieved by deleting items 1 and 2 and collapsing the response categories in item 8; however, this increased the ceiling effect to over 12%. In addition, some items displayed differential item functioning for important person factors such as age and disability level.

Conclusion: The FSS did not fit the Rasch model. Without fit, even the summed raw scores cannot be assumed to have ordinal level properties. Misfit could largely be remedied by deletion of poorly functioning items; but despite this, the scale did not appear to meet the stringent requirements of measurement which are desirable in outcome measures for clinical trials.

P2488
ROLE OF COGNITIVE DISORDERS IN MULTIPLE SCLEROSIS
N.F. Musina1, V.M. Alifirova2
Siberian State Medical University, Tomsk, Russia

Multiple sclerosis (MS) is the most venerable and important of the neurologic diseases. The results of the analysis of recent literature data demonstrate that cognitive dysfunction really exists both in patients suffered from relapsing-remitting MS and patients with secondary progressive MS, and it is characterized by a higher incidence than it has been presumed. Nevertheless, at the modern stage of the development of neurology, it is to be admitted that we know very little of the mechanisms conditioning cognitive disorders in MS. The aim of the study was to analyse the role of cognitive disorders in MS. Neurocognitive functions have been studied in 85 patients with MS. To study cognitive functions, the authors used the Mini-Mental State Examination, the California Verbal Learning Test, the frontal assessment battery, the procedure developed by A.R. Luriya. 85 patients with MS diagnosed according to McDonald’s criteria (McDonald WI et al., 2001) were examined: 27 males and 58 females aged 18–57 (mean age 33.4±7.8 yrs) with 1–16 yrs history of MS (mean duration 8.3±4.2 yrs). 59 patients suffered from relapsing-remitting MS, 26 patients were affected by secondary progressive MS. The degree of neurological deficit was estimated using the Expanded Disability Status Scale. Cognitive disturbances were detected in 61 (71%) patients. They included impairment of attention, planning, control, abstract reasoning, memory, special visual disorders.

Conclusion: The necessity to study the basic cognitive functions in MS.

P2489
A COMPARATIVE STUDY TO MEASURE EARLY AUDITORY RESPONSE (ABR) AND MIDDLE AUDITORY RESPONSE (MLR) WAVES BETWEEN PATIENTS WITH MULTIPLE SCLEROSIS (MS) AND HEALTHY SUBJECTS: A PILOT STUDY IN A GROUP OF IRANIAN MS PATIENTS
S.M. Nabavi1, M. Monadi2, G. Mohammadi-khan1
1Department of Neurology, Shahed University, 2Department of Audiology, Tehran University, Tehran, Iran

Objective: To measure characteristics of latency and amplitude of ABR waves I,III,V and of MLR waves Na, Pa, Nb in MS patients, and to compare them with normal subjects.

Methods: 31 definite MS patients according to revised McDonald criteria without obvious auditory complaints, and 31 matched normal subjects both with primary hearing threshold more than 50 db, underwent 2 Neurophysiologic studies of ABR and MLR measures.

Results: There were significant differences between the patients and control groups in ABR waves characterised as follows: average III peak latency was 4.85 in MS and 4.62 in normal groups (p=0.006). The average for V was 7.09 in MS and 6.63 in normal ones (p=0.06). Average inter-peak of I-III, III-V, I-V were 2.38, 2.24, 4, 62 in MS respectively and 2.15, 2.006, 4, 16 in normal groups respectively (p<0.05). Also in MLR measures there were significant differences between the two groups as follows: Na peak latency of MS patients was 22.75 and for normal groups was 20.85 (p=0.06). Pa peak latency of MS patients was 34.5 and for normal ones was 33.43. (p=0.139)

Conclusion: It seems both Neurophysiologic diagnostic tools of auditory domains show significant differences between MS patients and healthy subjects, and both methods can be used as
additional diagnostic measures, thought another study is needed to confirm superiority of one method.

Keywords: Auditory brain stem response, middle latency response, multiple sclerosis

P2490
OLIGOCLONAL IGG BANDS AND IGG INDEX IN THE CSF OF IRANIAN PATIENTS WITH MULTIPLE SCLEROSIS
M.R. Najafi, M. Reissfar
Department of Neurology, Medical School, Alzahra Hospital, Isfahan, Iran

Introduction: The cerebrospinal fluid oligoclonal IgG bands (OB) are less frequently observed in Iranian multiple sclerosis (MS) patients compared with Western country patients.

Methods: We studied 26 consecutive Iranian MS patients in order to investigate cerebrospinal fluid findings, and the differences in the clinical features of MS between OB-positive patients and OB-negative ones.

Results: Among the 26 patients IgG Index was higher than 0.7 in 21 (80.8%) and 15 (57.7%) patients were OB-positive and 11 (42.3%) patients were OB-negative. There were no differences between the 2 groups in the clinical forms of MS, gender, onset age, disease duration, disease severity and onset symptoms. The only near to statistically significant difference (0.08) in the MS group was the lower progression index (PI) observed in negative cases. However, IgG Index significantly correlated with PI (p<0.05, r=0.42).

Conclusion: We conclude that the frequency of positive IgG-OCB patterns in our MS patients is less than most values reported in the Western literature, and that negative results of IgG-OCB and low IgG Index indicate benign disease.

P2491
SEIZURES IN MULTIPLE SCLEROSIS (MS): ELECTROCLINICAL CORRELATIONS
A. Oliveros Cid1, A. Oliveros Juste1, M.A. Cid Lopez2, C. Pascual1, I. Perez Lopez-Fraile3, B. Anson3
1Servicio de Neurologia, Clinica Quiron Zaragoza, 2Servicio de Neurologia, Policlinica Sagasta, 3Servicio de Neurofisiologia, Clinica Quiron Zaragoza, Spain

Background: Epileptic seizures occur more frequently in patients with MS than in the general population, as we know since the earliest studies on this topic. We attempted to evaluate clinical evolution and response to pharmacological treatment in this group of patients.

Patients and methods: A retrospective study of 78 patients seen between 1996–2006, diagnosed of probable MS. Mean follow-up time at inclusion 7.9 years (range between 1 to 17). In all the cases included, we kept all the clinical information regarding follow-up period, confirmed by family or friends; plus neuroradiological (MRI) and paraclinic (laboratory (blood test, CSF)) information; and antiepileptic drugs (AEDs) used in each case.

Results: 6 patients suffered from confirmed epileptic seizures. EEG showed epileptiform abnormalities in all the MS patients with epilepsy. In the majority of patients, seizures were partial with secondary generalization, with 2 cases of status epilepticus. All cases were treated with AEDs, in monotherapy or bitherapy. 2 cases required switch to another AED due to lack of efficacy. One more case required switch to a different AED due to adverse effects.

Conclusions: Symptomatic epileptic seizures in MS can occur anytime in the course of the disease, even as the initial symptom. There is an excellent electroclinical correlation, showing epileptiform abnormalities in all the “positive” cases. Risk of developing epilepsy in our group of MS patients, after a 10-year follow-up period, has shown to be similar to that showed in previous studies and much higher than in the general population.

P2492
PROGNOSIS & TREATMENT OF SYMPTOMATIC EPILEPSY IN MS PATIENTS
A. Oliveros Cid1, A. Oliveros Juste1, M.A. Cid Lopez2, I. Perez Lopez-Fraile3, E. Barreiro4, N. Fayed6
1Servicio de Neurologia, Clinica Quiron Zaragoza, 2Servicio de Neurologia, Policlinica Sagasta, 3Servicio de Neurofisiologia, Clinica Quiron Zaragoza, 4Servicio de Neurologia, Hospital Miguel Servet, 5Servicio de Urgencias, Clinica Quiron Zaragoza, 6Servicio de Neuroradiologia, Clinica Quiron Zaragoza, Spain

Background: Epileptic seizures occur more frequently in patients with Multiple Sclerosis (MS) than in the general population, as we know since the earliest studies on this topic. We attempt to evaluate clinical evolution and response to pharmacological treatment in this group of patients.

Patients and methods: A retrospective study of 78 patients seen between 1996–2006, diagnosed of probable MS. Mean follow-up time at inclusion 7.9 years (range between 1 to 17). In all the cases included, we kept all the clinical information regarding follow-up period, confirmed by family or friends; plus neuroradiological (MRI) and paraclinic (laboratory (blood test, CSF)) information; and antiepileptic drugs (AEDs) used in each case.

Results: 6 patients suffered from confirmed epileptic seizures. EEG showed epileptiform abnormalities in all the MS patients with epilepsy. In the majority of patients, seizures were partial with secondary generalization, with 2 cases of status epilepticus. All cases were treated with AEDs, in monotherapy or bitherapy. 2 cases required switch to another AED due to lack of efficacy. One more case required switch to a different AED due to adverse effects.

Conclusions: Symptomatic epileptic seizures in MS can occur anytime in the course of the disease, even as the initial symptom. There is an excellent electroclinical correlation, showing epileptiform abnormalities in all the “positive” cases. Response to AEDs is good, even in monotherapy. Status epilepticus is related to advanced disease with secondary cognitive impairment. However, selection of the proper AEDs is still a controversial issue.

P2493
EVALUATION OF THE RELATIONSHIP BETWEEN TWO RELAPSE EFFICACY ENDPOINTS IN CLINICAL STUDIES OF DISEASE-MODIFYING THERAPIES FOR MULTIPLE SCLEROSIS
G.N. O’Neill1, C.H. Polman1, L. Kappos1, M. Yang1, A. Pace1, M.A. Panzara1
1Biogen Idec, Inc., Cambridge, MA, USA, 2VU Medical Centre, Free University Hospital, Amsterdam, The Netherlands, 3University Hospital, Basel, Switzerland

Background and aims: Alternatives to currently accepted primary endpoints have increased utility in clinical studies of treatments for multiple sclerosis (MS), owing to ethical concerns related to use of placebo. As shown in long-term follow-up of placebo-controlled studies, MS patients who delay active treatment
may have increased disability and a greater degree of brain atrophy compared with patients who are treated earlier in the disease course. Patients may be more willing to enter a placebo-controlled study if they are offered the option of switching therapy in the event of a relapse. However, this limits the use of the annualized relapse rate (ARR) as a primary efficacy endpoint, because patients who switch therapies can no longer provide data for the analysis of ARR. The purpose of this analysis was to evaluate the relationship between ARR and proportion of patients relapsing in clinical studies of MS.

Methods: Using data from the pivotal studies of intramuscular interferon beta (IFN)-1a, subcutaneous IFN-1a, IFN-1b, glatiramer acetate, and natalizumab in patients with MS, the effect of active treatment on the proportion of patients relapsing was compared with its effect on the ARR. Placebo group data were also analyzed.

Results: The percentage reduction in the proportion of patients relapsing was linearly related to the percentage reduction in ARR. Proportion of patients relapsing was linearly related to ARR in the placebo groups. These relationships can be demonstrated mathematically.

Conclusions: The proportion of patients relapsing provides an accurate and meaningful measure of relapse efficacy that is comparable to the ARR.

P2494
RELATIONSHIP BETWEEN SOMATOSENSORY EVOKED POTENTIALS AND UPPER LIMB MOTOR FUNCTION IN PATIENTS AFFECTED BY MULTIPLE SCLEROSIS


1Institute of Neurology, Catholic University, Roma, 2Institute of Neurology, University of Siena, Siena, 3Institute of Neurology, University of Catania, Catania, 4Institute of Neurology, Magna Graecia University, Catanzaro, 5Fondazione Don Gnocchi, Roma, Italy

Objective: The aim of this multicentre (Catania, Catanzaro, Roma, Siena) study is to multidimensionally evaluate the relationship among somatosensory evoked potentials (SEPs) parameters, patient’s perspective and clinical measures of the upper limb impairment in patients with Multiple sclerosis (MS).

Methods: We consecutively enrolled 39 MS patients. For SEPs we acquired N9, P14, N20 and N9-P14 and P14-N20 intervals. To evaluate the upper limb impairment we used a validated patient-oriented questionnaire (Disability Arm Shoulder Hand questionnaire-DASH) and a test of dexterity quantification measured by the physician as the 9 Hole Peg Test (9-HPT). Statistical analysis was performed by using the STAT-SOFT (OK-USA) package.

Results: Comparing upper limbs performance we observed that MS patients with undetectable N20 and P14 responses performed 9-HPT in a significant longer time than patients with detectable responses (p<0.0006 and p<0.001 respectively). Similarly, comparing patients with normal and abnormal SEPs, we observed a significant longer time to complete 9-HPT (p=0.00006) in patients with abnormal SEPs. Concerning the perspective of patients, as measured through DASH questionnaire, we observed significant differences in patients with undetectable P14 (p<0.01) and abnormal N9-P14 intervals (p<0.03).

Conclusions: Our data suggest that, in MS patients, SEPs were correlated with impairment of the upper limbs as evaluated by measuring motor task and as referred by the patients. In conclusion, the current results provide a further meaning to upper limb SEPs: when we observe a patient with abnormal SEPs we can infer that the patient has most likely a deterioration of motor performance in the upper limb.

P2495
OBSTRUCTIVE SLEEP APNOEA AS A CAUSE OF FATIGUE IN MULTIPLE SCLEROSIS


1Department of Neurology, Red Cross Hospital, 2Department of Respiratory and Critical Care Medicine, Sotiria Chest Hospital, Athens, Attiki, Greece

Fatigue is a common symptom of Multiple Sclerosis (MS) and has been attributed to variable causes, including sleep disorders. The objective of this study is to determine the role of sleep disordered breathing and particularly Obstructive Sleep Apnoea-Hypopnoea Syndrome (OSAHS) in the pathogenesis of fatigue in MS. 10 MS patients (age and sex matched) who suffered from fatigue and 10 MS patients with no fatigue symptoms underwent overnight polysomnography. The severity of fatigue was evaluated with the Modified Fatigue Impact Scale (MFIS). The measured polysomnographic variables included total sleep time / time in bed ratio, minimum oxygen saturation values and the Apnoea-Hypopnoea Index (AHI). AHI represents the number of disordered breathing events per hour during sleep, characterized by total (Apnoea) or partial (Hypopnoea) cessation of airflow at the nose and mouth. A minimal threshold of 5 obstructive breathing events per hour is used to diagnose OSAHS. (4 (40%) of our patients demonstrated high AHI values (10, 11, 18 and 28 respectively, mean 14.5±4.9), with concomitant presence of respiratory efforts during disordered breathing events, indicative of upper airway obstruction, a feature of OSAHS. None of the MS patients in the no fatigue group showed sleep disordered breathing. In conclusion, OSAHS may be a major factor contributing to fatigue in MS patients and polysomnography could be considered in cases with severe fatigue symptoms. Further investigation is necessary to ascertain the incidence of OSAHS in MS and clarify the pathogenic processes involved.

P2496
THE ROLE OF DIET IN EARLY RELAPSING REMITTING MULTIPLE SCLEROSIS – A RANDOMISED CONTROLLED SINGLE-BLIND PILOT STUDY (ONGOING CLINICAL TRIAL)

P.S. Shah, J.I. O’Riordan, L. Gold, G. Houston, P. Donnan

1Department of Neurosciences, 2Department of Nutrition and Dietetics, 3Department of Clinical Radiology, Ninewells Hospital, 4Department of Medical Statistics, Dundee University, Dundee, UK

Background: MS is an autoimmune disease of the CNS and the commonest causes of disability in young adults in the Western world. There is increasing evidence that nutritional factors and gut immunity have a role in autoimmune conditions. There is often evidence of malnutrition in patients with MS. A number of patients are on alternative diets but the scientific basis of this is often lacking. Current treatments for MS are unsatisfactory and the role of dietary intervention has been relatively under-explored in MS. Though dietary modifications are often difficult, and need major lifestyle changes, they provide a sense of empowerment to patients, giving them control and initiative in managing the disease. This study will compare the effects of the established advice of the MS Society with that of the alternative Best Bet Diet (a hypoallergenic diet high in vitamin-D).
Methods: 30 patients between age group of 18 to 55 with a diagnosis of MS, EDSS scores up to 3.5 will be randomised to the Best Bet Diet or the Dietary advice given by the MS Society. The patients will have frequent MRI scans and clinical assessments. The dietician will guide the patients through both dietary changes. The assessor will be blinded towards the dietary changes. Patients will also complete monthly symptom questionnaires, and food diaries. The duration of intervention is 12 months. The primary outcomes are white matter lesion load on MRI scans and rate of brain volume atrophy. Secondary outcomes are clinical measures and symptom scores.

P2497
PREVALENCE OF GUT PERMEABILITY IN MULTIPLE SCLEROSIS AND EVALUATION OF GUT PERMEABILITY WITH BEST BET DIET IN MS – A CONTROLLED PILOT STUDY (ONGOING CLINICAL TRIAL)
P.S. Shah¹, J.I. O’Riodan¹, L. Gold², S. Fleming³
¹Department of Neurosciences, ²Department of Nutrition and Dietsetics, Ninewells Hospital, Dundee, ³Department of Biochemistry, Royal Cornwall Hospital, Truro, UK

Background: MS is an autoimmune disease of CNS and affects young individuals. It is one of the commonest causes of disability in young individuals in the developed world. An environmental factor appears to be important in causing the disease in a genetically susceptible individual. This factor is yet to be identified. Gut plays an important role in immune tolerance and increased gut permeability can lead to the loss of food tolerance and heightened immune response. Food antigens can evoke local as well as systemic allergic response. Absorption of unprocessed food antigens may perpetuate autoimmune conditions due to molecular mimicry. Many patients with MS follow elimination diets and role of gut permeability in MS patients has not been studied.

Methods: Subjects with diagnosis of relapsing remitting MS as confirmed by McDonald’s criteria will be invited. 25 subjects and 25 healthy controls will undergo a triple sugar (Rhamnose, Lactulose, Sucralose) test to assess gut permeability. The subjects will undergo further dietary intervention with the hypoallergenic diet with high dose vitamin D supplements (Best Bet Diet) for 6 months and the triple sugar test will be repeated. The triple sugar urinary excretion test for gut permeability is a sensitive test for assessing permeability of small and large intestine. This pilot study will look at any differences of gut permeability in subjects with MS and healthy controls and will also look at effect of dietary intervention on the gut permeability in patients with MS.

Results: There was a reduction in the cervical cord size of 5.83% in the group on the whole: 9.60 mm before therapy (9.27–9.94, alpha=0.05); 9.04 mm after (8.70–9.39, alpha=0.05) (p=0.027). A significant difference in atrophy increased was found between treatment groups (H(2, N=30)=8.06 p=0.0178): the atrophy extent was less after therapy with Glatiramer acetate (3.51%) in comparison with Interferons-beta (7.00%) (p=0.02).

Conclusions: The serial measurement of spinal cord atrophy may make a significant contribution to the evaluation of therapeutic efficacy, further research could help to choose the best medication to prevent spinal atrophy.

P2498
DECELERATION OF THE ATROPHY OF THE CERVICAL SPINAL CORD IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS DURING IMMUNOMODULATING THERAPY
E.G. Shipova¹, N.N. Spirin¹, D.S. Kasatkin¹, E.I. Shumakov², I.O. Stepanov¹
¹Department of Neurology and Medical Genetics, Yaroslavl State Medical Academy, ²MRT Department, Railway Hospital, ³Department of Neurology #3, City Hospital #8, Yaroslavl, Russia

Background: There is not enough information about the natural history of the cervical atrophy in relapsing-remitting multiple sclerosis (RRMS) and its changes during immunomodulating therapy.

Methods: Magnetic resonance imaging (MRI) of the cervical spinal cord was made in 30 patients with definite RRMS, the mean age was 31.7 year (28.5–35.0, alpha<0.05), mean EDSS 2.7 (2.3–3.0), mean duration of MS 4.3 year (3.1-5.5). Scans were performed on a 1.5 Tesla MR-station “Signa Infinity HiSpeed”. T1 and T2-weighted images were obtained, the size of spinal cord was measured on sagittal slices at the level of the lower edge of C2-vertebra. The examination was made twice with a 14-months interval. During this period patients had received immunomodulating therapy (Interferon-beta 1a – 7 patients, Interferon-beta 1b – 13 pts, Glatiramer acetate – 10 pts). The programmes SPMS (MATLAB 7.0) and Jim 4.0 were used for processing of the images and morphometry.

Results: A significant difference in atrophy increased was found between treatment groups (H(2, N=30)=8.06 p=0.0178): the atrophy extent was less after therapy with Glatiramer acetate (3.51%) in comparison with Interferons-beta (7.00%) (p=0.02).

Conclusions: This paper analyzes the outcome of Mitoxantrone treatment in 20 patients with RR-MS and SP-MS conducted in The Clinic of Neurology during 2004–2006. Inclusion criteria were age 18–56, patients with RRMS with >2 relapses/year or S-P, with an EDSS increase >1/year, regardless of previous disease modifying therapy, EDSS at baseline up to 8. Exclusion criteria were blood haematological abnormalities, abnormal liver enzymes, concomitant potentially cardiotoxic therapy, cardiac diseases (VEF<50%), pregnancy. Patient evaluation consisted in anamnesis, clinical form assessment, number of relapses within the last 2 years, neurological examination (EDSS), 7.5 meter walk time. QoL (general status, degree of autonomy, mood, adverse events) performed at each visit. Para clinical evaluation included cerebral MRI before and after 1 year after therapy ECG, cardiac echography (VEF), blood haematology and liver enzymes before and 4 days after drug infusion. Mitoxantrone was administered i.v. every 3 months in saline perfusion (12 mg mitoxantrone/m² body surface) up to a total of 100–140 mg/m². The F/M ratio was 14:6 Age 35–53, 8 with RRMS (with a mean of 4 relapses in the last 2 years), 12 with SPMS, with a disease history of 4–19 years an EDSS 3–8 (mean 6). There was an overall benefit from the therapy, EDSS decreased in 7 patients no change in 8; and a 1-point worsening in 5; 4 patients were converted successfully to Betaferon. One serious adverse effect (acute thrombocytopenia) was signalized. All parameters of clinical and paraclinical evaluation are discussed.

© 2007 EFNS European Journal of Neurology 14 (Suppl. 1), 165–301
P2500
ANTIVIRAL THERAPY IN MULTIPLE SCLEROSIS PATIENTS WITH HERPES VIRUS PERSISTENCE
L. L. Sokolova, A.A. Kruglyak
Neurology Department, National Medical University of Ukraine, Kyiv, Ukraine

Aims: To compare the results of antiviral and traditional therapy in MS patients with herpes virus reactivation and to determine the advisability of antiviral therapy in MS patients with herpes virus persistence.

Methods: 50 MS patients, 19–46 years old, were examined. The mean EDSS score was 2.0–4.5 and the disease duration was never more than 5 years. The herpes virus activity was detected by polymerase chain reaction (PCR) and antibodies (Ab) – IgM and IgG to HSV1/2, CMV, EBV and HHV-6. The tests were done for both blood and CSF specimen.

Results: Positive DNA of one virus of a kind and the increased IgG titres to several herpes viruses were detected in all patients. Patients were randomized in two 25 people groups: basic therapy with neurometabolites and vasoactive drugs was administered to I group, and group II received basic therapy as well as aciclovir or cimeven i/v 5–10 mg/kg for 14 days and interferon medicine. Mean EDSS score in group I was 2.2, in group II – 2.8. 6 months after treatment mean EDSS score in group I averaged 2.5, in group II – 2.3 (p<0.001). The state of health of 14 patients of group I and 23 patients of group II had stabilized (p<0.001). One year after treatment, in group I there were 19 patients with exacerbations, in group II – 7 (p=0.012).

Conclusions: The results obtained show effectiveness of antiviral therapy in MS patients with active herpes virus persistence. This therapy decreases the amount of exacerbations and neurological deficit progress.

P2501
ASTHENIA AND FATIGABILITY IN MULTIPLE SCLEROSIS (MS): CORRELATION WITH BRAIN MRI FINDINGS
N.N. Spirin, D.S. Kasatkin
Department of Neurology, Yaroslavl State Medical Academy, Yaroslavl, Russia

Background and Objectives: Fatigue, a common and frequently disabling symptom in MS, is a complex syndrome that includes two different clinical entities: Asthenia (fatigue of rest) and Fatigability (fatigue of action). In this study, we tried to find specific MRI abnormalities of both syndromes.

Methods: 46 MS patients (aged 18–49 years; 14 men and 32 women) with the duration of the disease 1.0–9.6 years and EDSS score 1.5–4.0 were enrolled in the study. All individuals completed Malkova’s Asthenia Scale (AS), Multiple Sclerosis Fatigue Scale (MFIS) and were tested with Modified Tapping-test (MT), Paced Auditory Serial Addition Test (PASAT). Using MRI, we conducted voxel-based morphometry of brain with SnPM2 implemented in MATLAB 7.0 for analyzing. In the statistical process we applied nonparametric methods: Spirmen’s correlation analysis, Mann-Whitney U-test.

Results: Asthenia was determined in cases with moderate and high level of fatigue in both scales (AS, MFIS); isolated Asthenia was pointed out in 17.4%. Fatigability was recognized in cases of physical (MT) and/or psychical (PASAT) working capacity decreasing in 40%; isolated fatigability had been observed in 45.7%. Significantly higher summary lesion loads were found in patients with asthenia than in patients with fatigability (p=0.047); more significant difference was observed in comparison with lesions volume in periventricular trigone (p=0.035). Contrary, infratentorial lesion loads were higher in the group with fatigability (Up=0.053). Intensity of asthenia, but not fatigability, significantly increased with augmentation in volume of supratentorial (p=0.048) and periventricular (p=0.020) MRI lesions.

Conclusion: Fatigue in MS is a clinical diverse entity, showing different MRI findings.

P2502
ABSENCE OF SYMPATHETIC SKIN RESPONSE IN PATIENTS WITH MULTIPLE SCLEROSIS: ABSENCE OF CLINICAL IMPACT?
Th. Thomaides1, O. Tsika2, J. Rallis1, Y. Zoukos3, Th. Karapanayiotides4, A. Aspiotis1
1Department of Neurology, Greek Red Cross Hospital, 2Department of Neurology, Pammakaristos Perfuctural Hospital, Athens, Greece, 3Department of Neurology, Royal London Hospital, London, UK, 4Department of Neurology, Ipokratelion Hospital, Thessaloniki, Greece

Objective: To assess sympathetic skin response absence (SSR) in patients with multiple sclerosis (MS) and its possible association with disease duration, disability and MRI lesion location.

Methods: We evaluated SSR in the four limbs of 35 patients with definite MS (women: 26, age: 39±10.5 years, disease duration: 7.1±5.1 years, EDSS: 4.3±3.4). All patients had recent MRIIs of the brain and the cervical spinal cord. We examined the possible association of SSR absence with MRI lesion location, disease duration, disability and other patient characteristics.

Results: SSR was absent in at least one limb in 16 (46%) patients (SSR[-]; in one limb: n=5; in 2 limbs: n=5; in 4 limbs: n=6). 14 out of 16 patients with SSR[-] (87.5%) had MRI lesions in the cervical spinal cord compared to 12/19 (63%) patients with SSR present in all limbs (SSR[+]) (ANOVA, p=0.1). Inversely, the frequency of SSR[-] in patients with abnormal MRI of the cervical spinal cord was 54% (14/26) compared to 22% (2/9) in patients with normal MRI (ANOVA, p=0.1). Disease duration was longer (9.5±6.5 vs. 4±2.3, p=0.008) and disability tended to be greater (4.9±2 vs. 3.8±1.3, p=0.51) in SSR[-] vs. SSR[+] patients. Disease duration and disability were independently correlated with SSR absence in one or more limbs (p=0.01).

Conclusions: We suggest that SSR absence can not be used as a surrogate marker for the presence of MRI lesions in the cervical spinal cord. All patients should be screened and followed up with MRI. In newly diagnosed patients with MS, SSR absence may denote long-standing disease.

P2503
MITOXANTRONE THERAPY IN BALO CONCENTRIC SCLEROSIS
M. Vokaer1, D. Baleriaux2, J.C. Bier4
1Department of Neurology, 2Department of Neuroradiology, Erasme Hospital, Brussels, Belgium

Background: Balo concentric sclerosis (BCS) is a rare disorder typically presenting with subacute onset of progressive encephalopathy, brainstem, motor, sensory, or autonomic dysfunction. Majority of patients have monophasic course which leads to death within a few months. However, patients with a relapsing-remitting course suggestive of typical multiple sclerosis associated with cranial MRI demonstrating “Balo-like lesions” have been described. The etiology of BCS is currently unknown and there is no proven treatment for it. Since it is sometimes considered a variant of
multiple sclerosis, acute neurologic worsening has been treated with glucocorticoids. However, questions remain about the duration of therapy and long-term management with immunosuppressive agents.

Case report: A 25-year-old female patient presented walking difficulties and ocular motor impairment in January 2006. Brain MRI revealed white matter abnormalities suggestive of multiple sclerosis. CSF analysis demonstrated the presence of oligoclonal bands. EDSS was 3.5 and i.v. corticosteroid treatment was performed. 7 months later, after hospitalization for acute worsening of her disease, EDSS was 7.0 and another course of iv corticosteroids was performed. Brain MRI demonstrated concentric hypointense T1-weighted and hyperintense T2-weighted bands alternating with isointense white matter highly suggestive of Balo concentric sclerosis. 3 courses of i.v. Mitoxantrone 12 mg/m² + Methylprednisolone 1 g were then performed at monthly intervals and resulted in a stabilization of the EDSS at 6.0. Interferon beta-1b therapy was initiated in January 2007 while the EDSS was 6.0.

Conclusions: This case highlights the potential role of Mitoxantrone in the management of Balo concentric sclerosis.

P2504
UNUSUAL PRIMARY MANIFESTATIONS OF MULTIPLE SCLEROSIS
Y. Yetimalar, Y. Seçil, A. İnceoğlu, M. Başoğlu
Department of Neurology, Ataüürk Training and Research Hospital, Izmir, Turkey

Objectives: Our purpose is to describe the patients with unusual symptoms as primary manifestation of multiple sclerosis (MS).

Patients and methods: 22 MS patients presented unusual initial pictures (acute brachial pain n=4, headache n=6, ptosis n=1, ocular motor nerve palsy n=1, peripheral facial palsy n=1, Ramsay-Hunt syndrome n=1, throat pain n=1, hypoglossal nerve palsy n=1, visual field defect n=2, epilepsy n=2, and coma n=2) as the first manifestations in the absence of other obvious symptoms.

Results: 4 patients described radicular pain and arm weakness. 6 patients presented new onset headache. 1 patient had acute throat pain. 2 patients had acute ptosis. 2 patients presented with a facial palsy and Ramsay-Hunt syndrome. 1 patient noticed a difficulty in phonation and manipulating food due to central monoparesis of the tongue. 2 patients had homonymous hemianopia and monocular altitudinal defect. 2 patients developed late-onset seizures. 2 patients presented coma. None had previous medical or neurological disorders. Investigations demonstrated changes highly suggestive of MS on MRI, CSF and electrophysiological tests. All cases completely or partially recovered after corticosteroid therapy. These patients have been followed up for 5 years.

Conclusion: We discuss possible correlations between clinical and neuroradiological abnormalities and show some rare or previously undescribed manifestations in MS. The observation of rare manifestations in MS may guide us to understand the MS pathogenesis better.

P2505
IS AN OCCURRENCE OF NABS A PERMANENT MARKER OF DECREASED EFFICACY OF INTERFERONS?
D. Bartko, I. Combor, M. Boselova
1 Institute of Medical Sciences, Neurosciences and Military Health, 2 Central Military University Hospital, 3 Faculty of Health Sciences, Ruzomberok, Slovak Republic

P2506
CENTRAL NERVOUS SYSTEM DEMYELINATION ASSOCIATED WITH ACUTE INFLAMMATORY DEMYELINATING POLYNEURORADICULITIS – MS OR ADEM?
B. Barun, V. Brinar, I. Zadro
Department of Neurology, Referral Center for Demyelinating Disorders, University Hospital Center ‘Zagreb’, Croatia

P2507
EVALUATION OF CLINICAL FACTORS EFFECTS ON RESPONSE TO INTERFERON BETA-1-A IN PATIENTS WITH REMITTING RELAPSING MULTIPLE SCLEROSIS (RRMS)
N. Beladimoghadam, I. Bakhshande
Neurology Department, Shahid Beheshti Medical University, Imam Hossein Hospital, Tehran, Iran

P2508
COEXISTENCE OF MULTIPLE SCLEROSIS AND POLYMYOSITIS
M.H. Harirchian
Iranian Center of Neurological Research, Imam Khomeini Hospital, Tehran University of Medical Science, Tehran, Iran

P2509
MULTIPLE SCLEROSIS – ANALYSIS OF CLINICAL CHARACTERISTICS, FORMS AND PROGNOSTIC FACTORS
M.G. Manova, I.I. Kostadinova, T.V. Vassileva, A.I. Trenova
1 Department of Neurology, 2 Departments of Pharmacology, Clinical Pharmacology and Drug Toxicology, Medical University, Plovdiv, Bulgaria

P2510
DIFFERENTIAL DIAGNOSIS OF PAPPILEDEMA
M.N. Markov, Ks. Knteska, D. Georgiev, M. Milekova
Department of Demyelinating and Degenerative Diseases, St. Naum Hospital, Sofia, Bulgaria

P2511
ACUTE DISSEMINATED ENCEPHALOMYELITIS WITH ACUTE ABDOMINAL PAIN: A CASE REPORT
S. Ozakbas, D. Tosun, E. Idiman
Department of Neurology, Dokuz Eylul University, Izmir, Turkey
P2512

DEMYELINATING POLYNEUROPATHY ASSOCIATED WITH MULTIPLE SCLEROSIS: COINCIDENCE OR THE SAME PATHOGENESIS?

N. Subutay Oztekin1, M.F. Oztekin1, G. Orban1, F. Ak1
12nd Neurology Department, 1Neurology Department, SB DoSkap, Education and Research Hospital, Ankara, Turkey

P2513

SOME EXPERIENCE WITH INTERFERON BETA 1-B (IFN µ1-B) TREATMENT OF PATIENTS WITH MULTIPLE SCLEROSIS

Lj.B. Radulovic, S. Vujicic
Neurology Department, Clinical Centre of Montenegro, Podgorica, Montenegro

P2514

NEUROMYELITIS OPTICA AND PULMONARY TUBERCULOSIS: AN UNCOMMON ASSOCIATION

S.A. Siddiqi, M. Hashmi, K.A. Siddiqi
Department of Neurology, Liaquat National Hospital, Karachi, Pakistan

P2515

MULTIPLE SCLEROSIS AND ANTI-PHOSPHOLIPID SYNDROME WITH CNS INVOLVEMENT

Lj. Stancetic Bacvanin
Neurology Department, General Hospital, Sremska Mitrovica, Serbia

P2516

JEAN SIBELIUS DIED OF STROKE – THE PATHOGRAPHY AT THE 50TH ANNIVERSARY OF HIS DEATH

T. Breitenfeld, V. Vargek Solter, D. Breitenfeld, V. Supanc, V. Basic Kes, K. Jergovic, V. Demarin
Neurology Department, Sestre Miloradnice (Sisters of Charity) University Hospital, Zagreb, Croatia

The most renowned Finnish composer Jean Sibelius led a somewhat frenzied life. He composed, taught, conducted and played chamber music. However, sometimes all this was not enough to pay his debts. He had depressive states, therefore he consumed alcohol. One of the long time strong anxious-depressive states was probably on account of a suspected (and never confirmed) laryngeal cancer. On the other hand, he often laughed and was amusing company. Jean Sibelius was very famous during the second half of his life even though the last thirty years he almost did not compose anything. Peaceful way of life gave him a long age. He died at the age of 92 in relatively good health, suddenly, from stroke (cerebral haemorrhage). Sibelius had completed his musical opus many years before.

P2517

A HISTORICAL INQUIRY ABOUT PARASOMNIA DIAGNOSIS AND TREATMENT: AEGIDIUS OF ATHENS OR ELSE KNOWN AS SAINT GILLES

K. Koumakis1, M. Aggelou2
1Department of Neurology, Euroclinic of Athens, 2History of Medicine Department, University of Athens Medical School, Athens, Greece

St. Aegidius or Gilles was born in Athens in the 7th century in 640 A.D. into a noble family. He was forced to leave Athens to escape his increasing reputation of sanctity, due to his miraculous healings of neuropsychiatric diseases. He became famous as a hermit with miraculous powers in the treatment of parasomnias, sleep terrors and nightmares, mania and psychiatric diseases, which he included in the category of panic disorders. He settled in a province in France where he founded the monastery of Saint Gilles, which became a famous place of pilgrimage in the middle age period. After his death in 721, his tomb became a place of pilgrimage for believers suffering from sleep disorders. His tomb was rediscovered in 1865. Aegidius was probably the first to recognize parasomnias and to use the term “panic” to refer to this category of diseases. It derives from the name of the god Pan. The term panic was used to describe the symptoms provoked humans the appearance of Pan, which were: acute, dramatic and immediate terror, hair erection of his victims, even gods, nymphs and warriors were forced to run away. His victims were usually unsuspicious people, who were seized by his sudden appearance and his loud voice. After that experience they were afraid of a possible repetition of the same incident and they took precautions not to provoke the god Panas. It is remarkable that apart from his appearance and his loud voice, the god Pan had no other fearful weapon.

P2518

JEAN FRANCOIS LANGLAIS (1907–1991): A HISTORICAL CASE OF APHASIA AND BRAILLE ALEXIA WITHOUT AMUSIA

C.A.H. Fisher1, A.J. Larner2
1General Practice, Marches Surgery, Leominster; 2Cognitive Function Clinic, Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Objective: To report and contextualise the case of Jean Francois Langlaiss (1907–1991), a renowned French composer and organist, blind from the age of 2, who suffered a stroke at age 77 which caused aphasia without amusia and Braille alexia.

Method: Translation from French of the original paper describing the case (Signoret et al.; Rev Neurol Paris 1987;143:172-81).

Results: Left middle cerebral artery stroke affecting the temporoparietal territory resulted in fluent aphasia of Wernicke type with impaired comprehension and repetition, Braille alexia and agraphia for words. However, the patient was still able to play the organ, hum and sing tunes, read a musical score written in Braille, and eventually began composing again in Braille. Hence there was no Braille alexia or agraphia for musical notation, suggesting right hemisphere localization for these functions.

Discussion and conclusions: From the information reported in the original paper, this patient seems to have had an associative type agnosia causing Braille alexia for words but not for musical notes. He therefore differs from a recent case seen by one of the authors in which Braille alexia for words appeared to result from a subtle apperceptive tactile agnosia. There may be a spectrum of neuro-psychological deficits causing Braille alexia.
The famous scientist Prof. Korbinian Brodmann was born on 17 November 1868 in Liggersdorf, Hohenzollern in Germany. He studied medicine in Munich, Würzburg, Berlin and Freiburg and received his “Approval” in 1895. In 1898, Brodmann took his Doctorate in Leipzig with a thesis on chronic ependymal sclerosis. He met Alzheimer who inspired in him an interest in neuroanatomy at Municipal Mental Asylum in Frankfurt. In 1901, Brodmann joined Vogt in the Neurobiological Laboratory in Berlin. He suggested Brodmann to undertake a systematic study of the cerebral cortex cells, using sections stained with the method of Nissl. In 1903, Brodmann described a completely different cytoarchitectonic structure of the pre and postcentral gyri in humans and pointed border between them. The foundation of Brodmann’s cortical localization is a subdivision into areas with similar cellular and laminar structure. He distinguished 47 areas in humans, each marked with an individual number. He was an editor of the Journal für Psychologie und Neurologie, were he also published his major results. The journal lived on as the Journal für Hirnforschung and became the Journal of Brain Research in 1994. In 1909, Brodmann’s legendary book „Vergleichende Lokalisationslehre der Grosshirrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues“ was published. It remains the basis for functional localization of cerebral cortex, with Brodmann’s areas still extensively used. In 1918, Brodmann was appointed to Kraepelin’s newly formed Psychiatric Research Institute in Munich at the Department of Topographical Anatomy. On 17 August 1918, Brodmann developed pneumonia and on 22 August 1918, he died of septicaemia.

Stroke or apoplexy: apoplexy derived by Greek Apoplixia (to stun) or ictus by Latin ictu(m) (stroke). At the time of Hippocrates (460–370 BC) stroke was considered as a sudden burst mostly or ictus by Latin ictu(m) (stroke). At the time of Hippocrates (460–370 BC) stroke was considered as a sudden burst mostly or ictus by Latin ictu(m) (stroke). At the time of Hippocrates (460–370 BC) stroke was considered as a sudden burst mostly 

The “sacred disease” as described in the Hippocratic writings is often understood as the first description of epilepsy with tonic-clonic seizures. However, the pathology attributed to the sacred disease in classic antiquity is much broader than the description given by the author of the Hippocratic treatise, as it also comprises a wide spectrum of psychotic symptoms and behavioural abnormalities. Elements of this pre-Hippocratic concept of the sacred disease may be identified in the Greek literature of the 5th century B.C.: The sacred disease serves as a model of mental and behavioural dysfunction caused by supernatural powers. Thus, it is the ideal foil for the description of abnormal behaviour in classic Greek tragedy. The tragic poets use the symptoms and signs of the sacred disease to depict tragic heroes that have lost their sanity due to divine intervention. Thus, divine action as a supernatural cause of the hero’s mental disturbance immediately becomes obvious to the spectators of the 5th century B.C. From the 4th century B.C., a continuous differentiation between the concepts of epilepsy (epilepsy), mania (non-febrile psychotic diseases) and phrenitis (febrile diseases with psychotic symptoms) is observed in the medical treatises, and this development gradually enters public awareness. Thus, the Roman
tragedian Seneca (1st century A.D.) is able to rely exclusively on the description of psychotic symptoms to convey the impression of a tragic hero arbitrarily driven insane by divine powers.

P2523
HOWARD FLOREY’S RESEARCH ON THE CEREBRAL CIRCULATION
D. Todman
Department of Medicine, University of Queensland, Brisbane, QLD, Australia

Howard Florey is best known as the scientist whose research team at Oxford developed Penicillin and ushered in the modern antibiotic era. He was one of the foremost medical scientists of the twentieth century and achieved the highest honours including the Nobel Laureate with Chain and Fleming in 1945, a life peerage, the Order of Merit as well as becoming president of the Royal Society and chancellor of the Australian National University. His qualities as a medical scientist reveal a person of great vitality and drive who applied himself to diverse fields of experimental medicine and pathology. Florey’s initial research was in the years 1922–1925, when as a Rhodes scholar at Oxford he came under the tutelage of Sir Charles Sherrington who directed him in neuroscience research. Florey’s work on cerebral circulation began in Oxford under the supervision of Sherrington and continued in Cambridge during the tenure of the Walker studentship. The paper appeared in ‘Brain’ and was read at the Physiological Society in London and constitutes his first publication. Experiments on the convulsant Thujone on the cerebral cortex ran in conjunction. This paper analyses the original contribution to medical knowledge from his early scientific work. Sources from the Florey archive at the Royal Society highlight his close personal relationship with Sherrington and the important and discerning mentorship he displayed.

P2524
HENRY WOLTMAN, PIONEERING AMERICAN NEUROLOGIST
D.H. Todman
Department of Medicine, University of Queensland, Brisbane, QLD, Australia

Henry Woltman (1889–1964) was the first neurologist at the Mayo Clinic at a time when there were few practitioners working full-time in this field in North America. In the early 20th century the specialty of neurology began to flourish in a centre which was established by William Worrall Mayo in Rochester Minnesota in 1863. It became a multi-specialty medical centre under the impetus of Dr. Henry Plummer, an endocrinologist who commenced at Mayo in 1901. Henry Woltman qualified in medicine at the University of Minnesota and trained in neurology in Minneapolis where he gained a PhD for his research on the effects of pernicious anaemia on the brain. In July 1917 he moved to the Mayo Clinic and led the remarkable growth in this discipline for almost 40 years. The neurology section at Mayo Clinic is consistently recognised in the respected US News and World Report as number one ranking in its annual survey of North American medical centres. The professional life of Henry Woltman laid the groundwork for the development of Mayo neurology through 3 main areas namely; the close relationship of neurology to internal medicine rather than psychiatry, the development of a unique scoring and notation system and the close collaboration with neurosurgery. This paper analyses the leadership of Henry Woltman in these fields from a variety of published sources and material related to the early years of neurology at the Mayo Clinic.

P2525
LEVEL OF ANTIBODIES TO PHOSPHOLIPIDS IN PATHOGENESIS OF CRANIOCEREBRAL TRAUMA
M. Gerasimova, L. Ngankam
Tver State Medical Academy, Tver, Russia

Craniocerebral trauma (CCT) is widely occurring cause of neural disorders resulting in disability and lethal outcome. Aim of this study was to learn the level of antibodies to phospholipids (aP) in cerebrospinal fluid (CSF) in CCT.

Materials and methods: 100 patients in acute period of CCT (aged from 9 to 72 years; 73% male and 27% female) were investigated. Along with clinical, neurological and instrumental investigat- ion immunoassay was performed. Immunoassay included determination of aP level in CSF. Obtained results were compared with control group consisting of 30 persons.

Results: All patients according to clinical signs were divided into 3 groups: 1–62 pts with brain concussion (BC), 2–30 with cerebral contusion (CC) of middle grade and 3–8 with cerebral contusion of severe grade. Immunoassay showed in all cases higher aP level in CSF (0.095±0.002 unit optical density (UOD)) as compared to control group (0.02±0.001 UOD), p<0.001. In patients of group 1 aP level was 0.075±0.002 UOD, in pts of group 2 –0.098±0.002 UOD, in pts of group 3 – 0.25±0.01 UOD, p<0.001. Therefore, direct correlation between aP level in CSF and severity grade of CCT has been found.

Conclusion: Correlation between aP level in CSF and CCT severity was found. APs are markers of vessel endothelium affection. This may suggest that aP is involved in pathogenesis of CCT.

P2526
A PILOT NEUROIMAGING STUDY EVALUATING EFFECTS OF MEMANTINE ON BRAIN VOLUME, GLUCOSE METABOLISM AND COGNITION – A RANDOMISED, DOUBLE-BLIND, PLACEBO – CONTROLLED DESIGN IN ALZHEIMER’S DISEASE
R. Schmidt1, St. Ropele2, B. Ebenbauer3, M. Windisch4, A. Stößler5, F. Fazekas6
1Department of Neurology and Division of Neuroradiology, Department of Radiology, Department of Neurology, Medical University Graz, 2JSW-Research GmbH, Graz, Austria, 3Department of Neurology, Medical University Graz, Austria, 4Merz Pharmaceuticals, Frankfurt am Main, Germany, 5Department of Neurology, Medical University Graz, Austria

Objective: Memantine’s neuroprotective abilities were shown in different preclinical studies. In the present study the aim was to evaluate the effects of memantine on different neuroimaging parameters recognised as markers for neuroprotection. These were in particular the brain volumetry and metabolism in patients with mild to moderate Alzheimer’s disease (AD).

Methods: Of 37 randomized patients, 32 completed the imaging evaluation after 6 months and 24 after 12 months. Efficacy assessments were defined as changes in whole brain and hippocampal volume and changes in metabolic activity. Clinical outcome measures were ADAS-cog, ADCS-ADL and CDR.

Results: Due to the pilot character of this study and the small sample size the differences remained non-significant. Nevertheless memantine-treated patients showed a numerical improvement relative to placebo in all clinical outcome variables (ADAS-cog, MMSE, CDR, ADCS-ADL). The memantine group showed a
similar loss of total brain volume compared to placebo patients, although the memantine treated group had substantially less reduction in hippocampal volume at weeks 26 and 52. No differences between memantine and placebo treated groups were seen with respect to NAA and myoinositol concentrations. PET assessment after 52 weeks of treatment showed less decrease of cerebral glucose metabolism in all brain regions in memantine-treated patients than in those receiving placebo.

Conclusions: Clinical effects seen in the study were consistent with previous clinical trial results. Smaller loss of hippocampal volume in patients treated with memantine is in line with the suggested neuroprotective effect of the drug. A reduced decrease in glucose metabolism supports beneficial functional effects.

P2527
THE LOW RATE OF CHRONIC POSTCONCUSSION SYMPTOMS, FOLLOWING MILD HEAD INJURIES IN GREEKS: A PROSPECTIVE STUDY
P.C. Spinis1, G.C. Sakellaropoulos2, A.G. Deli3, T.G. Maraziotis1, C.D. Constantoyannis1
1Department of Neurosurgery, Patras University Hospital,
2Department of Medical Physics, Medical School of Patras,
University of Patras, 3Department of Ophthalmology, Patras University Hospital, Patras, Greece

Background: The prevalence of symptoms following mild head injury (MHI) varies in a number of studies, often 20–40% of subjects still report symptoms after 3 months, and 15% after 1 year. The objective of this study is to determine the characteristics and the incidence of symptoms in these patients and estimate the incidence of post concussion syndrome in a Greek population.

Methods: A prospective examination of patients with MHI, presented in the Emergency Department of Patras University Hospital, was performed. The study included 200 adults. The GCS score on admission was 14–15. All the patients had an initial neurological examination. The patients were re-examined after 1, 3 and 6 months. We developed a post concussion symptom checklist that included the same items used by our group in a previous study. The patients were asked to describe their symptoms during the follow-up period of 6 months.

Results: A brain CT-scan was necessary in 57% of the patients. There were 9% CT-detected intracranial lesions, like contusions (3%), haematomas (1%), head fractures (4%). The most common symptom at the initial examination was headache (73%), followed by dizziness (31%) and memory loss (22%). Six months after injury the incidence was significantly lower – headache (3%) – dizziness (6%).

Conclusion: In Greece, despite the frequent experience of minor head injury, there is a very low rate of post concussion symptoms 6 months after the injury. The cultural difference regarding symptom expectation might explain the low rate of chronic symptoms in Greeks.

P2528
PROTECTIVE ACTION OF ADENOSINE TRIPHOSPHATE (ATP) ON LOCAL COMPRESSION INJURY OF A BRAIN AND SPINAL CORD
G.Z. Sufianova1, A.G. Shapkin1, A.A. Sufianov1, Yu.G. Shapkin1, M.V. Taborov2, A.N. Mahov3, M.A. Yusina2
1East-Siberian Scientific Centre of Siberian Branch, The Russian Academy of Medical Science, East-Siberian Neurosurgical Centre, 2State Medical University, 3Institute of Solar-Terrestrial Physics, The Siberian Branch The Russian Academy of Science, Irkutsk, Russia

The purpose of research was to study neuroprotective action of ATP on local compression brain and spinal cord injury. The work is carried out on 25 rats weighing 180–220 g. The ATP was injection intracerebroventricularly in a dose of 1 mg/kg and intraperitoneally in a dose of 50 mg/kg (30 minutes before injury). For an estimation of the functional state of a nervous tissue spent simultaneous registration of slow electric activity (EEG and electrospinogram), and DC potential. Registration of bioelectric activity was spent by Ag/AgCl electrodes by unipolar technique with a DC gauge amplifier of 1 T Ohm in-pit resistance. Compression injury modelled on the local disposed compression of a brain. The data was statistically analyzed with use of the T-test and the U-test. Preventive introduction of ATP was accompanied by a decrease of amplitude and rate of depolarization, and also increase of functional restoration during the posttraumatic period. At intracerebroventricular injection of ATP more significant changes were recorded. The mechanism of decrease of ischaemic depolarization at brain injury, on a background of ATP action, can be explained to reduction of metabolic needs of a nervous tissue on a background of a hypoxia and a hypoglycemia (ischaemia). Therefore, rising reserve opportunities of the nervous cells is marked, allowing going through a longer period of damage.

P2529
DIFFERENCES IN HIPPOCAMPAL MR FINDINGS WITH WHITE MATTER SUPPRESSION SEQUENCE IN MCI AND ALZHEIMER’S DISEASE USING 3 TESLA MRI
J. Takahashi1, S. Takahashi1, H. Yonezawa1, M. Kudo1, S. Obara1, T. Shibata2, M. Sasaki2, T. Inoue1, Y. Terayama2
1Department of Neurology, 2Department of Radiology, 3Department of Neurosurgery, Iwate Medical University, Morioka, Iwate, Japan

Background and aims: Cognitive ability among patients with Alzheimer’s disease (AD) declines in almost the same manner as the disease progresses. The pathology of AD has been thoroughly investigated, while neuroimaging techniques have limited its possibility mainly due to their resolution. To visualize and compare regional gray matter cell density of hippocampus, entorhinal area and substantia innominata using 3 Tesla (3T) MRI in patients with AD or mild cognitive impairment (MCI), inversion recovery (IR) sequence was employed.

Methods: Subjects were 43 patients with AD, 10 patients with MCI and 12 controls. All scans were performed using a Signa VH/I 3.0 Tesla MR imaging system. We employed IR sequence (TR 4000 ms, TE 20 ms, TI 250 ms) to suppress white matter signals and emphasize gray matter signals. Using gray matter emphasized image, ROIs were positioned on CA1, subiculum, entorhinal area and substantia innominata and their intensity were measured.

Results: The intensity in subiculum and entorhinal areas significantly decreased compared with CA1 (p<0.05) at the beginning of MCI stage. On the other hand, intensity of substantia innominata, which was unchanged during MCI stage, declined after FAST (Functional Assessment Staging) IV stage of AD (p<0.05).

Conclusions: By using 3T MRI, detailed morphological changes of hippocampus, entorhinal area and substantia innominata can be visualized. Furthermore, this method enables us to observe longitudinal changes of those structures from MCI to AD patients. We believe this is a powerful tool to elucidate AD etiology and to evaluate the efficacy of anti-AD drugs including acetylcholinesterase inhibitor.
P2530
AUTONOMIC DYSREGULATION INCREASES THE DEVELOPMENT OF HETEROTOPIC OSSIFICATION IN SEVERE TRAUMATIC BRAIN INJURY: A PROSPECTIVE STUDY
P.J. van Kampen¹, J.D. Martina¹, A. Pos², P.E. Voos³, H.T. Hendricks²
¹Rehabilitation Centre Groot Klimmendaal, Arnhem, ²Department of Rehabilitation, ³Department of Neurology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Introduction: Heterotopic ossification (HO) is a frequent complication in traumatic brain injury (TBI) and may lead to serious comorbidity. In this study we investigated factors including coma duration, mechanical ventilation, spasticity, fractures, immobilization, systemic infection and autonomic dysregulation for their ability to predict the occurrence of HO.

Method: All TBI patients with a GCS ≤3 admitted to the Radboud University Nijmegen Medical Centre between Jan 2004–July 2006 were included.

Subjects: 176 consecutive patients were included, 74 died within 3 months post-injury. HO was defined as bone formation in soft tissue resulting in clinical symptoms like pain and limitation of ROM, confirmed by radiography. For coma duration, ventilation duration, systemic infection, autonomic dysregulation, spasticity and fractures we calculated the relative risks using HO as outcome variable.

Results: Of the 102 patients studied (78% male), mean age was 38 years (range 16–83). The incidence of HO was 11.7%. Age, GCS at admission, ICP and CPP were not statistically different between patients developing HO or not. HO patients had a longer duration of coma (13.13 versus 6.64 days, p=0.001), and were longer mechanically ventilated (16.00 versus 9.68 days, p=0.007) compared to those without. Autonomic dysregulation was the only factor that significantly increased the risk for HO (relative risk 5.75, CI=2.03-16.24).

Conclusions: Patients with HO had sustained the most severe brain injuries as demonstrated by longer coma- and ventilation duration compared to patients without. Autonomic dysregulation further increased the risk for HO.

P2531
PERFORMING A MULTI-CENTER IMAGING STUDY TO EVALUATE THE EFFECTS OF MEMANTINE ON THE RATE OF BRAIN ATROPHY IN PATIENTS WITH ALZHEIMER’S DISEASE (AD)
N. Fox¹, D. Wilkinson, P. Scheltens², F. Barkhoff², R. Phul³
¹Dementia Research Centre, Institute of Neurology, London, ²Memory Assessment and Research Centre, Moorgreen Hospital, Southampton, UK, ³VU Medical Center, Amsterdam, The Netherlands, ³Landbeck Limited, Caldecote, Milton Keynes, UK

AD is characterised by cognitive decline and progressive brain atrophy. Atrophy can be used as an indirect marker of cellular pathological processes occurring in AD. Serial MRI registration is a sensitive, reliable, well-validated method for monitoring rates of cerebral atrophy in AD patients. The NMDA antagonist memantine has been shown to have neuroprotective effects in preclinical studies. The objective of the current 52-week multi-centre study (protocol 10112) is to use MRI to explore the effects of memantine on the rate of brain atrophy in patients with probable AD (NINCDS-ADRDA criteria) during 1 year of treatment. Approximately 300 patients (MMSE 12-20 incl; age≥50 years) are being randomized equally (1:1) to receive memantine (10 mg/BID) or placebo. The boundary shift integral technique is being used to assess direct changes in total brain volume (TBV). TBV change is selected as it includes all potential areas of brain loss and quantification is automated. Multiple MRI scans of the patients, at screening, week 4, 42, and 52, will improve precision in estimating cerebral atrophy rate. Verbal fluency tests (COWAT and category fluency), Stroop, orientation and Neuropsychiatric Inventory are being used to evaluate cognitive and behavioural outcomes. In this poster, we will discuss the optimal study design, timing of scans to maximise power, methodology used to evaluate TBV and quality control processes for evaluation of the MRI. These processes include careful evaluation of MRI scanners, refined screening of patients to exclude other factors influencing the TBV analyses and involvement of independent imaging experts to monitor the scan quality.

P2532
CHANGES IN GRAY AND WHITE MATTER IN MILD COGNITIVE IMPAIRMENT USING 3T MRI
H. Yonezawa¹, S. Takahashi¹, J. Takahashi¹, M. Kudo¹, S. Obara¹, T. Shibata¹, M. Sasaki¹, T. Inoue¹, Y. Terayama¹
¹Department of Neurology, ²Department of Radiology, ³Department of Neurosurgery, Iwate Medical University, Morioka, Iwate, Japan

Purpose: To investigate the differences of gray and white matter integrity in mild cognitive impairment (MCI) from those among normals and patients with Alzheimer’s disease (AD).

Subjects and methods: Gray matter intensity in several regions of interest (ROI) was measured, utilizing white matter suppression sequences MRI (TR/TE: 4000/16.5, TI=250 ms) among 10 patients with MCI, 18 patients with AD and 10 normals. Relative intensity ratio (gray matter value / cerebellar value) was compared among MCI, AD, and normals. Fractional anisotropy (FA) value in several ROI reflecting the integrity of the white matter nerve fibers was measured utilizing diffusion tensor MRI (b=2000) among 14 MCI, 10 ADs, and 10 normals. ROI were set and measured on several white matter regions.

Results: Among AD patients, relative intensity ratios in hippocampal head, anterior cingulated gyrus, inferior temporal gyrus and posterior cingulate gyrus were significantly decreased compared to those among normals (p<0.05). Among MCI patients, relative intensity ratios in inferior temporal gyrus, hippocampal head and anterior cingulated gyrus were significantly decreased compared to those among normals (p<0.05). Among AD patients, FA value in temporal and angular subcortical white matter, internal capsule, posterior cingulated bundle, frontal subcortical white matter and trunk of corpus callosum (p<0.05) were decreased compared with normals, while no significant differences were observed in FA value between MCI and normals.

Conclusion: The above data suggests that cortical degeneration in hippocampal head and inferior temporal gyrus precedes degeneration in posterior cingulate gyrus and white matter changes among patients with MCI.

P2533
CAROTID ARTERY TORTUOSITY AND WHITE MATTER CHANGES IN HYPERTENSIVE STROKE PATIENTS: A 3 DIMENSIONAL ARTERIAL PATH TRACKING BY MR ANGIOGRAPHY
K.H. Yu¹, I.S. Koh², S. Jung¹, Y.G. Min¹, H.J. Seo¹, M.S. Oh¹, B.C. Lee¹
¹Department of Neurology, Hallym University, Sacred Heart Hospital, Anyang, Kyanggi, ²Department of Neurology, National Medical Center, Seoul, South Korea
**Background and aims:** Vascular structural changes related to longstanding hypertension include elongation or tortuosity of the arteries. White matter hyperintensities (WMHs) on MR imaging may also be the result of hypertensive vasculopathy in the intracranial small vessels. We examined the relation between ICA tortuosity and WMHs on MRI in hypertensive stroke patients.

**Methods:** We quantified the tortuosity of ICA in 73 hypertensive stroke patients using a 3-dimensional path tracking method from reformat image of MR angiography. The tortuosity was expressed as tortuosity index which was the ratio of total length of winding paths of artery relative to the direct distance from bifurcation to cavernous portion of ICA. We graded WMHs quantitatively using the visual rating scales of Scheltens, and dichotomized them to the high (n=39) and low grade WMH group (n=34) by 50% of subjects according to Scheltens scale. The ICA tortuosity, demographic features and vascular risk factors were compared within 2 groups.

**Results:** ICA tortuosity in hypertensive stroke patients is significantly, but modestly correlated with WMHs on MR imaging (spearman correlation r=0.403, p<0.001). Age and ICA tortuosity index (1.363±0.153 vs. 1.503±0.135, p<0.001) were significantly different between 2 WMHs groups. In multivariate analysis adjusting for age, sex, and other vascular risk factors, ICA tortuosity index remained significant (multiple logistic regression, P=0.005).

**Conclusions:** The geometrical deformities of ICA in hypertensive stroke patients correlate with the white matter changes. The tortuosity of ICA might represent hypertensive arteriopathy as primary vascular etiology, like WMHs on MRI.

**P2534**

**MR SPECTROSCOPY IN PATIENTS WITH HEREDITARY SPASTIC PARAPAREGIA TYPE SPG4**

A.K. Erichsen¹, A. Server³, P.H. Nakstad², C.M.E. Tallaksen¹

¹Department of Neurology, ²Department of Neuroradiology, Ullevål University Hospital, Oslo, Norway

**Background:** The hereditary spastic paraplegias (HSP) are heterogeneous neurodegenerative disorders, characterized by progressive spasticity and weakness in the lower limbs. Axonal loss in the long corticospinal tracts has been shown in HSP-patients. However, supraspinal symptoms and findings in patients linked to the most common dominant HSP-type, SPG4, support the theory that the disease also causes neuronal cerebral damage.

**Objective:** To investigate whether SPG4-HSP leads to early neuronal biochemical changes detectable on MR-spectroscopy (MRS).

**Material and methods:** Single-voxel proton MRS of the brain was performed in 8 patients from 4 families with genetically confirmed SPG4-type HSP and 8 healthy age- and sex-matched controls. Volume of interest (VOI) was located in the frontal white matter and in the precentral gyrus (motor cortex). The following ratios were calculated for both locations: NAA/Cr, NAA/Cho, Cho/Cr and ml/Cr.

**Results:** The choline to creatine ratio (Cho/Cr) in SPG4-HSP patients showed a significant reduction (p = 0.047) in the motor cortex compared with controls, suggesting reduced membrane turnover as result of cell loss. In addition NAA/Cr in cerebellar white matter tended to decline and ml/Cr to increase in the HSP subjects, suggesting progressive neuroaxonal loss in the white matter.

**Conclusion:** Proton MRS proved to be a useful investigational tool for detection of metabolite abnormalities in areas of the brain that appeared normal on MRI. Cho/Cr could be a surrogate marker of neurodegenerative process in SPG4-HSP.
brainstem ischemic stroke in 1 case. Myelitis involvement with hyperintense lesions was found in 1 case. Brain-MRI was normal in 1 case.

**Conclusion:** MRI is a very sensitive diagnostic method and the investigation of choice for (NB) disease. This study investigates the correlation between clinical, MRI findings, and follows the literature data about the predilection of mesodiencephalic lesions.

**P2537**

**ANATOMICAL REGIONS MEDIATING NEURO-PSYCHIATRIC SYMPTOMS IN DEMENTIA**


1Neurology Department, General Hospital of Athens, 2Nuclear Medicine Department, "Alexandras" University Hospital of Athens, Athens, 3Department of Statistics, University of Piraeus, Greece

**Aim:** To correlate the neuro-psychiatric symptoms of dementias with regional cortical perfusion.

**Methods:** 65 patients participated in the study from an outpatient Memory Clinic. All of them had a neuropsychological evaluation and the neuro-psychiatric symptoms measured by the Neuro-Psychiatric-Inventory. 30 were diagnosed as Fronto-temporal Dementia and 35 -that of Alzheimer’s disease according to established criteria. All of them had a single photon emission computed tomography (SPECT) with 99mTc-HM-PAO. In the maps that derived from the scanner we measured the Cerebral Blood Flow (CBF) in regions of interest (ROI) across the cortex. We used as reference the CBF of visual cortex as it is the least and probably the last to be affected by the above diseases. We divided the CBF of every ROI to that of the reference region and we accepted as pathological any value below 0.8. The ROIs are 10 on every frontal lobe, 4 on every parietal lobe, 2 on every temporal lobe and 7 across the middle line for both hemispheres (5 frontal, 2 parietal).

**Results:** From correlation analysis (Spearmann) we found statistical significant correlation of 7 neuro-psychiatric symptoms with r-CBF

- Delusions: posterior-parietal regions
- Agitation: frontal regions on both hemispheres
- Depression: temporal regions
- Apathy: right frontal regions
- Disinhibition: left orbitofrontal region
- Aberrant Motor Behavior: left frontal and temporal regions
- Euphoria is decreased with hypo-perfusion in left premotor region

**Conclusion:** The data support the involvement of both hemispheres (more the right) in mediating social and emotional behaviour, and that distinct regions regulate different behaviours.

**P2538**

**A DIFFUSION-WEIGHTED MRI FINDING IN A PATIENT WITH HEAT STROKE IN THE ACUTE PERIOD**

J.H. Kwon, A.H. Cho

1Department of Neurology, Ulsan University Hospital, Ulsan, 2Department of Neurology, St. Mary’s Hospital, Seoul, South Korea

Heat stroke is a life-threatening illness characterized by cerebral dysfunction such as delirium, convulsions or coma resulting from elevated core body temperature above 40°C. Several reports showed delayed cerebellar atrophy or failure of microcirculation. However, brain MRI findings have not been sufficiently studied. Moreover, a diffusion-weighted image (DWI) finding was never reported. A 40-year-old man was admitted because of decreased consciousness after seizure-like movement. He was working outside, the temperature of 33°C. When he arrived at the local hospital, he had developed seizure-like movements which subsided with cooling and hydration. His body temperature at arrival was 41°C, which fell 38°C after cooling. On physical exam after 7 hours attack, generalized petechia were observed on the chest. Vital signs were unremarkable except high body temperature. There was no focal neurological deficit except stuporous consciousness. Routine laboratory test showed markedly elevated muscle enzyme suggesting rhabdomyolysis. On DWI taken after 13 hours from onset, high signal intensity lesion was observed on the right corona radiata, which was also a high signal on T2-weighted image. However, on the apparent diffusion coefficient map, there was no signal change. He became alert 10 hours after admission with medical management such as hydration and cooling. We report a patient with heat stroke who had lesion on the right corona radiata on DWI in acute period which is supposed to be vasogenic oedema rather than cytotoxic oedema. In the early period of heat stroke with cerebral dysfunction, therapeutic strategy for reducing vasogenic oedema should be considered.

**P2539**

**NEUROIMAGING FINDINGS IN PATIENTS WITH TRAUMATIC BRAIN INJURY CAUSED BY SEIZURES**

I.M. Lipko

Department of Urgent Medicine, Kiev Medical Academy of Postgraduate Education, Kiev, Ukraine

**Background:** Patients with epilepsy have an increased risk of traumatic brain injury (TBI). The aim of our study was to investigate the neuroimaging findings in patients with TBI caused by seizures.

**Methods:** CCT and MRI investigations in 110 patients with TBI due to seizures (96 male and 14 female) with mean age of 36.9 years were compared with 100 control patients with TBI without preliminary seizures.

**Results:** Most patients had mild TBI. In structure of TBI prevalence concussion 57.2% and subdural haematoma 26.4%. Signs of contusio cerebri were found in 15.4%, intracerebral haematoma only 1%. Epidural haematoma was not found. Atrophy signs with changes in liquor pathways were the most frequently determined in patients with TBI due to seizures. With statistically significant difference the presence of hydrocephalus externus in this category of patients (p<0.01) was estimated.

**Conclusions:** The findings of the present study add more detailed information about neuroimaging features in patients with TBI due to seizures towards improvement of our knowledge.

**P2540**

**SURGICAL TREATMENT OF THE SKULL BASE AFTER INJURIES**

V. Matejcík

Department of Neurosurgery, Medical Faculty of Comenius University, Bratislava, Slovak Republic

The aim of this study is the presentation of 3 cases of reconstructive surgery of the skull base after craniofacial injury.

**Injuries and methods:** Fractures of the skull base represent 5–20% of all craniofacial injuries. Liquorea occurs in 11% of these cases, for frontobasal injuries associated with orofacial injuries up to 36%. Extensive injuries of the skull base result in communication with paranasal cavities.

**Diagnostics:** The most serious part of the operation is the isolation of the liquor space from the external environment. Reconstruction surgeries of the skull base have significantly improved in recent years due to development of new methods in diagnostics and treat-
P2541
MORPHOLOGICAL CHANGES OF THE HUMAN PURKINJÉ CELLS AND DEPOSITION OF NEURITIC PLAQUES AND NEUROFIBRILLARY TANGLES ON THE CEREBELLAR CORTEX OF ALZHEIMER’S DISEASE
I.A. Mavroudis1, K.I. Tsamis1, D.G. Mytilinaios1, A. Safouris1, S.N. Njau1, D. Psaroulis1, V. Costa1, S.J. Baloyannis1
1Laboratory of Forensic Medicine and Toxicology, Aristotelian University of Thessaloniki, Greece

Alzheimer’s disease constitutes one of the main causes of cognitive impairment in the presenium and senium. The neuropathological spectrum of Alzheimer’s disease includes neuronal loss, as well as loss of dendritic spines, neurofibrillary degeneration and neuritic plaques mainly in the hippocampus and the cortex of the cerebral hemispheres. However, a limited number of neuritic plaques and minimal neurofibrillary tangles, considerable decrease in number of granule and Golgi cells in the granule layer, loss of Purkinje cells and synaptic alterations of the mossy fibres, granule cell dendrites, parallel fibres and Purkinje cell dendritic spines have been reported by previous studies. This study is based on the morphologic analysis of the cerebellar cortex of 6 individuals via silver impregnation (Golgi method and Gallyas staining). The morphological analysis revealed deposition of neuritic plaques, neurofibrillary tangles and loss of secondary dendritic branches, decrease in the density of their dendritic arborization and significant loss of dendritic spines of the Purkinje cells from Alzheimer’s brains in contrast to normal controls.

P2542
BRAIN MR VOLUMETRY IN PATIENTS WITH RHEUMATOID ARTHRITIS
L. Peterova1, Z. Masin1, J. Krasensky1, K. Peterova1, C. Dostal1, J. Vencovsky1, V. Peterova1
1MR Department, Radiodiagnostic Clinic, 1st Medical Faculty, 2Faculty of Mathematics and Physics, 3Institute of Rheumatology, 1st Medical Faculty, Charles University, Prague, Czech Republic

Aim of the study: We measured volumes of brain and lesion load in patients with rheumatoid arthritis (RA) in magnetic resonance (MR) images.

Patients and methods: We prospectively investigated 12 female RA patients and 12 healthy age- and sex matched controls by 1.5 T MR during year 2006. In all patients we investigated T2 weighted images in Turbo spin echo and fluid attenuated inversion recovery (FLAIR) sequence in 1mm slices in transversal plane. Measurements in special program Scanview began by alignment of all slices in space. Detail and noise were lowered by 3×3×3 Gauss2 filter. After separation of brain parenchyma from other intracranial tissues by manual contouring of inner brain, the inner brain volumes were counted in a relative signal intensity (SI) level of 3500. Pathological hypersignal lesions in FLAIR (above 8000 SI level) were determined in white matter equilibrated to 5000 SI level.

Results: Total average volume in patients group was 1209.58 cm3 (in 30–49 aged patients 1234.79 cm3, in 50–66 aged patients 1133.96 cm3). Total average lesion load was very low: 0.58 cm3 (in 30–49 aged patients 0.06 cm3, in above 50 years 0.75 cm3).

Conclusions: Brain volumes and pathological lesion load obtained by MRI of RA patients did not differ statistically from healthy volunteers’ data. The study was supported by research project MZO 00064165 and grant NR8459-3.

P2543
INVESTIGATION OF NEUROPSYCHIATRIC LUPUS PATIENTS WITH COGNITIVE DEFICIT
K. Peterova1, Z. Masin1, C. Dostal1, L. Peterova1, L. Podrazilova1, J. Krasensky1, V. Peterova1
1MR Department, Radiodiagnostic Clinic, 1st Medical Faculty, 2Faculty of Mathematics and Physics, 1Institute of Rheumatology, 1st Medical Faculty, Charles University, Prague, Czech Republic

Aim of the study: To investigate neuropsychiatric lupus patients (NPSLE) with cognitive deficit (disorders of memory, attention, visuospatial perception anomalies).

Patients and methods: A cohort of 50 NPSLE patients with cognitive deficit were studied (40 females, 10 males, average age 39.3 years) by laboratory screening, standard EEG 1.5 T magnetic resonance (MR) in T1- weighted, T2- weighted and flow attenuation inversion recovery. The foci were rated by their size, localization and type.

Results: 38 patients (76%) had EEG abnormalities. Focal EEG changes (40%, n=20) were non-specific and unrelated to any particular type of epilepsy or other symptomatology. Episodic abnormalities (16%, n=8) were slightly predominant in patients with intense recurrent cephalic, ictus and cognitive disorders but without specific correlation with clinical complaints. Diffuse EEG abnormalities (20%, n=10) correlated with a history of generalized tonic-clonic paroxysms. MR findings were pathological in all patients as supratentorial foci up to 3 mm in size, predominantly in the frontal and parietal lobes subcortically. Periventricular and infratentorial foci were less frequent.

Conclusions: NPSLE patients with cognitive disorders showed mainly focal non-specific EEG changes. MR foci were found mostly at the site of long cortico – subcortical pathways, corresponding to cortical functional disorders as seen in scalp EEG. MR abnormalities were non-specific, statistically significantly correlated neither to laboratory pathology, clinical state nor EEG abnormalities. EEG abnormalities were found in 76%, MR abnormalities in 100% of the group. The study was supported by research project MZO 00064165 and grant NR8459-3.

P2544
PECULIARITIES OF CEREBRAL AND LIVER METABOLISM IN PATIENTS WITH TYPE 1 DIABETES MELLITUS: AN 1H MRS STUDY
Z.Z. Rozhkova1, O.E. Lipskaya2, B.N. Man’kovsky2
1Department of Radiology, Medical Clinic: BORYS, Institute of Endocrinology, Academy of Medical Sciences of Ukraine, Kyiv, Ukraine

Background and aims: We propose MRS markers of type-1 diabetes mellitus.

Methods: 2 groups of patients are studied by 1H MRS with 1.5T Magnetom Vision (SIEMENS). The 1st group includes 60 patients (19–65 y.). The 2nd group has 75 controls (18–73 y.). 1H spectra in the brain and in the liver are recorded with SVS- and CSI methods.

Results: In the 1H spectra of the brain, the following signals are identified: NAA (2.02 ppm), Cr (3.03 ppm), Cho (3.24 ppm), Glx (19–65 y.), Cho (3.24 ppm), Glx
(3.43, 3.8 ppm), mlns (3.58 ppm), and Lac (1.33 ppm). From the 1H spectra of liver, the following signals are obtained: Cho (3.2 ppm), Lip (2.0 ppm), Glc (3.5–4.0 ppm), Lac (1.3 ppm). For the patients of the 1st group, the significant decrease of NAA and Cr and the increase of Cho, mlns and Glx peak areas are observed. Presence of Lac is characteristic for the diabetic state in the cases when the blood sugar content is more than 12 mM/L. The signals of Glx and Lac in the spectra of the liver of diabetics are detected more frequently compared to the spectra of volunteers. For the 1st group, these observations reflect the loss of capability of the greater portion of the liver to regenerate. That leads to the decrease of the oxidative pathway of metabolism and to the increase of glycolysis and accumulation of Lac.

Conclusions: MRS gives a new insight into brain and liver biochemistry in chronic and acute diabetes mellitus and is useful in evaluating the disturbances of metabolism in patients with long-term diabetes.

P2545

GENDER DIFFERENCE AND AGING EFFECT OF CORPUS CALLOSUM IN KOREAN ADULTS AND THE STUDY OF THEIR FUNCTIONAL SIGNIFICANCE

J. Ryu1, I.J. Rhyu1, K.W. Park1, D.H. Lee1
1Department of Neurology, Hanil Medical Center, 2Department of Anatomy, 3Department of Neurology, College of Medicine, Korea University, Seoul, South Korea

The sexual dimorphism and change with aging of corpus callosum is an ongoing dispute. Many other investigators report on the aging effect of CC have not been concluded. Because there are no conclusive data about these, we investigate if normal Korean adult’s CC, using MRI, shows changes in gender difference and aging. To study the sexual dimorphism and aging effect of CC, we analyzed the midsagittal MRI morphometry in 239 adults. Total area, sub-area, height, length, and five specific angles of the CC were analyzed. The subjects were composed of 108 young group (3rd decade; male: 51, female: 57) and 131 old group (7–8th decade; male: 60, female: 71). The selected images were analyzed with NIH Image. The area, linear parameters were measured with V-Works program. In the young group, gender differences, were observed in the area of splenium and length. The young male CC have larger splenium and longer length than female. Angle B was wider in females compared to males in young group. Angle A, C, D showed gender difference in old group. In aspect of aging effect, the shrinkage of CC area was observed with aging (Angle A: increase, Angle C: decrease, angle D: increase) This study reports Korean standard CC data based on healthy neurologically normal adults. These results can be useful to various fields including neuroanatomy, neuroradiology.

P2546

CRANIAL NERVES AND VERTEBRAL BASILAR ARTERIAL SYSTEM RELATIONS – ANATOMICAL AND IMAGING STUDY

E. Tarta-Arsene1, A. Marinescu2, M. Enyedi1, O. Tarta-Arsene1
1Anatomy Department, University of Medicine and Pharmacy Carol Davila, ‘University Emergency Hospital, ‘Clinical Hospital Alexandra Obregia, Bucharest, Romania

Purpose: The importance of anatomy is emphasized by steady development in imaging techniques. Our goal was to expose intimate relations of cranial nerves with branches of vertebral-basilar vascular system.

Methods: We compared anatomical dissections with MRI investigations in which we demonstrate close relations of cranial nerves to branches of the vertebral basilar arterial system.

Results: There are at least 95 variations of vertebral basilar arterial system branching described. As our work progressed we focused on following pairs of cranial nerves: III, IV, V, VI, VII, VIII, IX, X. The relations we emphasized through thorough anatomical dissection and MRI investigation tried to cover most of these variations in order to explain some important syndromes in which cranial nerves may be involved for example trigeminal neuralgia.

Conclusions: Anatomy and imaging techniques may clearly explain neurovascular conflicts with significant improvement in diagnostic procedures.

P2547

CLINICAL USEFULNESS OF DIFFUSION WEIGHTED MR STUDY WITH APPARENT DIFFUSION COEFFICIENT CALCULATION IN PATIENTS WITH MULTIPLE SCLEROSIS

G. Witkowski1, R. Poniatowska2, W. Sobczyk3, A. Rudnicka4, D. Ryglewicz1
11Department of Neurology, 2Department of Neuroradiology, Institute of Psychiatry and Neurology, Warsaw, Poland

Purpose: The aim of the study was to assess the practical value of DWI and ADC calculation in patients with multiple sclerosis (MS) on the low tesla open system.

Materials and methods: 66 patients (44 women, 22 men, mean age 33.4±9.9) with diagnosed and confirmed MS were enrolled in this study. In 52 cases relapsing remitting (RR) type of MS was diagnosed, in 10 cases – secondary progressive (SP) type, and in 4 cases primary progressive (PP). 23 (13 women, 10 men, mean age 31.4±11.1) volunteers were present in the control group. The MR study (axial plane FLAIR, DWI (b-value 0 and 600) and T1 weighted scan after contrast injection) were performed on the low tesla open MR system. The mean ADC value of unchanged white matter of temporal and frontal lobes was calculated.

Results: In 52 MS patients FLAIR showed the presence of hyperintensive foci in white matter. In 28 cases focal changes were also present in DWI. Enhancement after contrast was observed in 11 cases. The mean value of ADC in patients with focal changes was 119.47±1.05, in controls 109.21±2.13 (p=0.0024, t-test). The mean value of ADC in MS patients without changes in white matter was 111.3±1.8, and was not significantly different from the mean value in the control group (p=0.624, t-test)

Conclusion: ADC is significantly higher in SM patients with the presence of hyperintensive foci in white matter. ADC in SM patients without changes in MR did not differ from ADC value in healthy volunteers.

P2548

CORRELATION BETWEEN SIZE OF ISCHEMIC CHANGES IN PERFUSION COMPUTER TOMOGRAPHY IN THE ACUTE PHASE OF STROKE AND THE SIZE OF THE ISCHEMIC LESION IN A CONTROL CT

G. Witkowski1, P. Richter2, H. Jarosz3, A. Rozenfeld4, R. Poniatowska2, D. Ryglewicz1
11Department of Neurology, 2Department of Neuroradiology, Institute of Psychiatry and Neurology, Warsaw, Poland

Background: Perfusion CT (PCT) is used to estimate the size of an ischemic lesion in patients with acute stroke, when no or subtle
changes are present in plain CT. Moreover, PCT allows defining the core (an area of tissue necrosis) and the potentially reversible ischemia (penumbra).

**Methods:** PCT was performed on 16 patients admitted to the hospital during 12 hours after the onset of the symptoms. Wintermark and Michel (2002, 2005) criteria for assessment of ischemia were applied (MTT > than 145% of the contralateral side, core – rCBV is < 2 ml/100gm, and penumbra – rCBV is >2ml/100gm). After 7 days plain CT was made to estimate the final ischemic lesion.

**Results:** Mean NIHSS at an admission was 14.5 (from 5 to 22). No, or discrete changes were observed in admission plain CT. PCT shown ischemic changes of various size in the area of Medial Cerebral Artery (MCA). Core was present in all cases and its area was from 20% to 66% of the total ischaemia. CT made 7 days after the onset of the symptoms showed the presence of an ischemic lesion closely related to the changes observed in PCT. Size of the lesion was 80–92% of the ischemic area in PCT.

**Conclusion:** The area of ischemia in PCT was similar to the localisation of final ischemic lesion present in control CT 7 days after stroke. The size of ischemia in PCT correlated with clinical status, and was a good predictor of the severity of the stroke.

**P2549**

**EVALUATION OF FUNCTIONAL STATUS DURING BETA-INTERFERON THERAPY**

I. Zavoreo, M. Lisak, Z. Tikanjec, M. Bošnjak-Pašić, N. Blažič Čop, V. Demarin

Neurology Department, UH Sestre Milosrdnice, Zagreb, Croatia

The aim of the study was to evaluate impact of beta interferon therapy on functional status in MS patients. We included in our study data of twenty patients (11 female and 9 male) with remitting relapsing multiple sclerosis (RRMS). 13 patients were treated with interferon beta-1a (6 MIU 3 times weekly) and 7 patients with interferon beta-1b (9.6 MIU every other day). The Expanded Disability Status Scale (EDSS) was recorded before interferon therapy, 6 months and 1 year after initiation of interferon therapy. The mean EDSS score was slightly lower after 6 months and one year of interferon therapy in both groups, but the difference was not statistically significant (p=0.17 and p=0.14 in interferon beta-1a group and p=0.36 and p=0.18 in interferon beta-1b group). Results in this small group of patients showed early improvement in the functional status of multiple sclerosis patients during interferon therapy. Further follow-up is required to get additional information on the course of functional improvement in multiple sclerosis patients after a prolonged period of interferon therapy.

**P2550**

**CLINICAL AND MRI FEATURES OF NON-ALCOHOLIC WERNICKE’S ENCEPHALOPATHY**

G.Q. Fei1, C.J. Zhong1,2, L.R. Jin1, J. Wang2,3, Y.H. Zhang1, X.M. Zheng1, Y.W. Zhang1, Z. Hong2,3

1Department of Neurology, Zhongshan Hospital, 2Department of Neurology, Shanghai Medical College, 3Department of Neurology, Huashan Hospital, Fudan University, Shanghai, China

**Objective:** In order to pay more attention to non-alcoholic Wernicke’s encephalopathy (NWE) and to reduce delayed diagnosis or misdiagnosis of this disease.

**Methods:** We retrospectively reviewed clinical and cranial MRI data of all 12 cases of NWE admitted to Zhongshan hospital from 1999 to 2006 and analyzed the prognosis after administration of thiamine.

**Results:** Clinical manifestations of NWE were complicated and most of them were of no specific value diagnosis. Cranial MR and FLAIR imaging exhibited the correlation between the prognosis of the disease and the damage area of the brain. Typical MRI features showed increased T2W and FLAIR signal symmetrically surrounding the aqueduct and third ventricle, at the floor of fourth ventricle, and within the medial thalamus. In patients with deep coma, increased T2W and FLAIR signs were found in the regions of the cortex. We found 2/3 patients with strengthened signal of the mammillary bodies by contrast medium and all patients without atrophy. Cortex damage may be indicative of irreversible damage and poor prognosis.

**Conclusion:** NWE lacks characteristic clinical manifestation and is easy to be misdiagnosed. Cranial MR and FLAIR imaging has great value diagnosing NWE and to judge the prognosis of this disease.
P2554
NEUROIMAGE FINDINGS INDUCED BY COCAINE
G. Garcia-Martín1, J.A. Hernández-Pérez1, N. García-Casares1,
J. Vega-Pérez2, E. Vila-Herrero1, C. De la Cruz-Cosme1,
V. Serrano-Castro1, R. Aguilar-Cuevas1, M.J. Gomez-Heredia1,
F.J. Garzon-Maldonado1, M. Romero-Acebal1
1Department of Neurology, 2Department of Radiology, Hospital
Virgen De La Victoria, Malaga, Spain

P2555
BRAIN MRI FINDINGS IN ATAXIA TELANGIECTASIA
M. Habek1, V.V. Brinar1, M. Rados1, I. Zadro1
1Department of Neurology, 2Department of Radiology, Zagreb School
of Medicine, Zagreb, Croatia

P2556
LUMBAR PUNCTURE VERSUS CISTERNA MAGNA
PUNCTURE IN RATS: A BLOOD CONTAMINATION
REPORT
I. Zamzuri1, P. Azim1, J. Abdullah1
1Department of Neurosurgery, Hospital University of Ghent,
Ghent, Belgium, 2Department of Neurosciences, School of Medical
Sciences, University Sains Malaysia, Kelantan, Malaysia

P2557
DUPLICATE ORIGIN OF THE LEFT VERTEBRAL
ARTERY IN TEENAGERS: ESTIMATION AND
DIAGNOSTICS THROUGH DUPLEX SCANNING
AND MAGNETIC RESONANCE ANGIOGRAPHY.
REPORT OF TWO CASES
M.I. Khristoforova, D.Y. Komkov, G.K. Panuntsev,
J.V. Nazinkina, N.E. Ivanova
Russian Research Polenov Neurosurgical Institute, St. Petersburg,
Russia

P2558
VERTEBRAL ARTERY DISSECTION WITH
RETROGRADE FLOW FROM BASILAR ARTERY
S.I. Lee1, H.D. Yang1, I.H. Son1, J.H. Kim1
1Department of Neurology and Inam Neuroscience Center, Sanbon
Hospital, Wonkwang University School of Medicine, Kun-Po,
Gyeonggi-Do, South Korea, 2Department of Neurology, Guro
Hospital, Korea University School of Medicine, Seoul, South Korea