

## Posters, Monday, October 28

### Cerebrovascular diseases 2

P 2001

#### Extreme hyperlipidemia is associated with increased intima-media thickness of the common carotid artery in patients below 55 years of age

T. Magyar<sup>1</sup>, G. Paragh<sup>1</sup>, A. Valikovics<sup>2</sup>, L. Csiba<sup>1</sup>, D. Bereczki<sup>1</sup>  
<sup>1</sup>University of Debrecen, Debrecen, HUNGARY, <sup>2</sup>County Hospital, Eger, HUNGARY

**Background** Contradictory results have been reported on the role of serum cholesterol and triglyceride in carotid atherosclerosis. As one of the reasons of the conflicting conclusions could have been the inclusion of mild and borderline cases, we measured intima-media thickness (IMT), a marker of atherosclerosis in patients with marked hyperlipidemia.

**Patients and methods** 29 patients with markedly increased serum cholesterol or triglyceride values in their history and 32 controls were compared. Blood samples for serum triglyceride, cholesterol, and homocysteine were taken after an overnight fast. Bilateral IMT measurements were performed in the common carotid arteries. Frozen enlarged images were used for online and offline evaluation. ANOVA was used for statistical analysis.

**Results** Patients with pure hypercholesterolemia (n=8) as well as patients with hypercholesterolemia and associated hypertriglyceridemia (n=21) had significantly higher serum cholesterol than controls (9.5±1.8, 9.2±3.0 and 5.0±0.7 mmol/L). There was no significant difference in serum homocysteine among the groups. Common carotid artery IMT was significantly larger in the hyperlipidemic groups than in controls (controls: 0.72±0.10 mm, pure hypercholesterolemia: 1.05±0.32 mm, combined hypercholesterolemia and hypertriglyceridemia: 0.97±0.17 mm; p<0.001).

**Discussion** Severe hypercholesterolemia is associated with increased IMT of the common carotid artery. The combination of hypertriglyceridemia with hypercholesterolemia does not result in an additional increase of IMT. Increased IMT in marked hypercholesterolemia cannot be attributed to increased homocysteine levels.

P 2002

#### Arterial blood pressure changes during acute and subacute stroke

G. Tsvigoulis<sup>1</sup>, E. Tzavellas<sup>2</sup>, P. Konstantopoulou<sup>2</sup>, A. Synetos<sup>2</sup>, V. Kotsis<sup>2</sup>, K. Spengos<sup>1</sup>, K. N. Vemmos<sup>2</sup>  
<sup>1</sup>Dept of Neurology, University of Athens Medical School, Athens, GREECE, <sup>2</sup>Dept of Clinical Therapeutics, University of Athens Medical School, Athens, GREECE

**Introduction** Elevated blood pressure (BP) values during acute stroke are widely reported. Aim of this study was to examine possible BP changes during the acute and subacute stroke stages for the different etiopathogenic stroke subtypes by means of 24 hour BP monitoring.

**Methods** 24 hour BP monitoring was performed during the 1<sup>st</sup>, 7<sup>th</sup> and 90<sup>th</sup> day after symptom onset in 69 first-ever stroke patients (12 cases with atherosclerotic large vessel disease, 8 cardioembolic strokes, 17 patients with small vessel disease (SVD), 17 cases of intracerebral haemorrhage (ICH) and 15 cases of unidentified cause). These findings were statistically compared with the data of 26 control persons (hypertensives without stroke) using One-Way-ANOVA and t-test.

**Results** When initially (1<sup>st</sup> day) compared with control, patients of all stroke subtypes showed significantly higher BP (p<0.001). A significant reduction (p<0.01) of the mean systolic BP between 1<sup>st</sup> and 7<sup>th</sup> day was described in all stroke subgroups, whereas a further significant decline (p<0.05) between 7<sup>th</sup> and 90<sup>th</sup> day was only seen among patients with ICH. The differences between corresponding recordings in the control group were not statistically significant. Patients with SVD presented in all 3 BP-recordings higher BP values than the control persons.

**Conclusions** During the acute stage, all stroke subtypes show elevated BP values, which seem to decline during the first week after stroke onset in all stroke subgroups. 3 months a further BP decrease is only observed in patients with ICH, whereas only patients with SVD show constantly higher BP values than control persons.

P 2003

#### Significance of peripheral blood nitric oxide initial data in acute ischemic stroke

M. Z. Beridze, R. R. Shakarishvili, M. I. Alpaidze  
State Medical Academy of Postgraduate Education, Tbilisi, GEORGIA

**Introduction** Accumulated evidences suggest that transducing mechanisms of NO-generation not only adapted to cytotoxicity, but also refer to cell protection.

Objective to define the nitric oxide levels in peripheral blood during 48 hours of ischemic stroke onset and to establish their correlation toward the outcome of disease at 1 month.

**Methods** 85 patients, aged 45 to 75, 38 male, 47 female have been investigated. NIHSS and Glasgow Coma Scale (GCS) assessed basic neurological impairments. Patients were divided into 3 groups according to severity of disease. I–group – 36 patients (NIHSS>15, GCS (9), II–group – 21 patients (NIHSS=10–15, GCS>9), III–group – (NIHSS<10, GCS=15). Barthel Index (BI), and Glasgow Outcome Scale (GOS) scored outcomes at 1 month. Controls consisted of 32 healthy individuals, aged from 40 to 70. NO levels were measured applying the electron paramagnet resonance (EPR) and spectrophotometer methods. The mean values computed by paired t-tests. The strength of association between the normally distributed variables defined using the Pearson Product-Moment Correlation Coefficient.

**Results** Peripheral blood NO levels during first 48 hours of acute phase were significantly lower in severe stroke patients compared to controls (62.7 versus 105.5 (15.9)) and correlated with poor outcome (R=+0.796 P<0.02), while the II and III

groups showed the elevated levels of NO (146.5 (3.93) 159 (31.4 respectively  $P < 0.01$ )) correlating with better functional outcome.

**Conclusion** The long-lasting NO generation in peripheral blood during critical stage of ischemic stroke is directed toward the activation of endogenous protective mechanisms.

#### P 2004

##### Evaluation of leukoaraiosis in stroke patients

O. Coskun, H. Yildiz, U. Emre, U. Akin, S. Ucler, T. Tunc, L. Inan

Ankara Hospital, Ankara, TURKEY

**Introduction** Pathogenesis of leukoaraiosis (LA) is not clearly understood. LA can be observed in patients with stroke. Significance of LA in patients with stroke remains undetermined.

**Methods** In Neurology Department of Ankara Hospital, Computed Tomography (CT) examination of brain was performed for various reasons in 288 patients from January 2000 to January 2001. LA was detected in 178 patients by the use of CT of brain. These patients were compared with the non-LA group. Student's *t* test and Pearson's  $\chi^2$  analysis were used for statistical analysis.

**Results** Patients with LA had a higher incidence of hypertension history (70.8%) when compared with the non-LA group (57.3%;  $p < 0.05$ ). There was no statistically significant difference in terms of sex, mean age, smoking, diabetes mellitus, history of cerebrovascular disease, cardiac failure, and ischemic cardiac disease between patients with and without LA. There was no statistically significant difference in the ratio of cerebrovascular disease severity and death between two groups.

**Conclusion** We showed that LA is related with hypertension but not related with age, diabetes mellitus and cardiac disease in our patient population.

#### P 2005

##### Microalbuminuria and hyperthermia independently predict long-term mortality in acute ischemic stroke patients.

W. Turaj, A. Slowik, A. Szczudlik  
Jagiellonian University College of Medicine, Krakow,  
POLAND

**Introduction** We designed this study to investigate the association between microalbuminuria (MA) and hyperthermia in acute ischemic stroke and to evaluate their significance as the predictors of long-term mortality after stroke.

**Methods** We studied 60 patients admitted within 24 hours after the onset of their first ischemic stroke. The Scandinavian Stroke Scale on admission and on day 1 assessed neurological deficit. Urinary albumin excretion was measured immunonephelometrically in 24-hour collection of urine performed on day 2. Body temperature was measured using infrared aural thermometer every four hours after admission on day 0, 1 and 2 and hyperthermia was defined as the body temperature  $> 37.5^\circ\text{C}$ . Outcome was assessed by 90-day and one-year mortality.

**Results** MA was found in 46.7% of patients. Hyperthermia was found in 18.3% patients on day 1 and in 25% patients on day 2. The correlation between albuminuria on day 2 and the body temperature on day 1 and on day 2 was found ( $r = 0.45$ , and  $r = 0.30$ , respectively; both  $P < 0.05$ ). The mortality was higher in the group of patients with both MA and hyperthermia on day 2 (73% vs. 10% after 90 days;  $P < 0.0001$  and 73% vs. 18% after one year,  $P < 0.005$ ). In the logistic regression analysis, albuminuria ( $P = 0.017$ ), hyperthermia on Day 1 ( $P = 0.028$ ) and neu-

rological deficit on admission ( $P = 0.044$ ) independently predicted one-year mortality after ischemic stroke.

**Conclusion** Daily albuminuria correlates with increased body temperature in acute stroke patients, but both these variables independently predict one-year mortality after ischemic stroke.

#### P 2006

##### Anterior ischemic optic neuropathy as first symptom in a patient with CADASIL

A. Rufa, M. Dotti, N. De Stefano, M. Stromillo, F. Sicurelli, S. Bianchi, A. Federico  
Neurology, Siena, ITALY

CADASIL is a cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, caused by Notch 3 mutation that lead to an abnormal accumulation of Notch 3 protein within the vasculature. Although CADASIL is considered a systemic arteriopathy prevalently affecting the central nervous system, pathologic changes consisting in granular osmophilic material (GOM) within the basement membrane of smooth muscle cells, have been shown on skin, muscle or nerve biopsy. An early involvement of both choroidal and retinal vasculature has recently been suggested also in asymptomatic CADASIL patients. We report on a 60 year old Italian man with subcortical dementia and family history of strokes, in whom clinical and molecular diagnosis of CADASIL was performed. The patient experienced at the age of 27 years an acute visual loss due to NAION. Diagnosis of CADASIL should be ruled out in young patients with acute ischemic optic neuropathy, absence of risk factors or associated conditions and family history of stroke.

#### P 2007

##### U-shaped relation of admission blood pressure values and early or late stroke mortality

G. Tsvigoulis<sup>1</sup>, K. Spengos<sup>1</sup>, P. Konstantopoulou<sup>2</sup>, A. Syntetos<sup>2</sup>, V. Kotsis<sup>2</sup>, K. N. Vemmos<sup>2</sup>

<sup>1</sup>Dept of Neurology, Medical School, University of Athens, Athens, GREECE, <sup>2</sup>Dept of Clinical Therapeutics, Medical School, University of Athens, Athens, GREECE

**Aim** Data on the prognostic significance of blood pressure (BP) levels following acute stroke are conflicting. We tried to evaluate a possible relation between admission systolic BP (SBP) or diastolic BP (DBP) and early or late mortality in the different groups of acute stroke patients.

**Subjects and methods** We studied a consecutive series of 1121 patients with first-ever acute stroke admitted to our hospital. Stroke was classified as ischemic and hemorrhagic stroke. Casual supine BP was measured at hospital admission. The mortality rate after 1 and 12 months was calculated in percentage and then analysed in relation to admission SBP, DBP and stroke type. Mortality rate was compared between the groups of SBP, DBP using the log-rank test. A two-tailed probability value of less than 0.05 was considered significant.

**Results** Distribution of stroke mortality 1 and 12 months after stroke in overall, ischemic and hemorrhagic stroke patients shows a typical U-shaped curve. However, the optimal SBP and DBP range for survival (U-point of the curve) for patients with ischemic stroke (SBP: 121–140 mmHg; DBP: 81–90 mmHg) was significantly lower ( $p < 0.01$ ) than for patients with intra-cerebral haemorrhage (SBP: 141–160 mmHg; DBP: 101–110 mmHg).

**Conclusions** Our results suggest that BP-values at admission are of prognostic relevance. It seems that the optimal initial SBP and DBP values for patients with ischemic stroke are lower than those for patients with hemorrhagic stroke. If these findings get prospectively verified, this may lead to a differentiated therapeutic approach of BP in acute stroke patients, depending on the type of stroke.

#### P 2008

##### **Apolipoprotein E genotypes and serum lipids and outcome after cerebral ischemia**

G. Gromadzka<sup>1</sup>, M. Baranska-Gieruszczak<sup>2</sup>, A. Ciesielska<sup>2</sup>, I. Sarzynska-Dlugosz<sup>2</sup>, T. Mendel<sup>2</sup>, A. Czlonkowska<sup>1</sup>

<sup>1</sup>Institute of Psychiatry and Neurology, 2nd Dept. of Neurology, Warsaw, POLAND, <sup>2</sup>Medical University of Warsaw, Dept. of Experimental and Clinical Pharmacology, Warsaw, POLAND

Apolipoprotein E (ApoE) polymorphism influences plasma lipids levels. Higher plasma cholesterol was associated with a better outcome after ischemic stroke (IS).

**Aim and method** To test the relationship between ApoE genotypes and serum lipids and outcome after IS, we examined ApoE genotypes (PCR RFLP method) in 169 IS patients.

**Results** Distribution of genotypes was: E3/3: 69.2%, E3/4: 14.8%, E2/3: 13.6%, E2/4: 2.4%. Patients carrying E2/3 genotype had lower plasma low-density lipoproteins (LDL) (121.4+/-28.6mg/dL), total cholesterol (TC) (183.6+/-25.8 mg/dL), and TC/high density lipoproteins (HDL) ratio (4.5+/-1.1mg/dL), as compared with E3/3 (LDL: 136.0+/-38.3mg/dL, p=0.04; TC: 202.0+/-46.5mg/dL, p=0.08; TC/HDL ratio: 5.2 +/-1.6 mg/dL, p=0.02), and E3/4 (LDL: 148.9+/-46.9mg/dL, p=0.03; TC: 217.3+/-60.3mg/dL, p=0.07; TC/HDL ratio: 5.7 +/-1.6mg/dL, p=0.009) genotypes carriers. As compared with "the lack of E2" genotype, allele E2 carriage was associated with decreased TC (p=0.03), LDL (p=0.01) and TC/HDL ratio (p=0.004). The allele E 4 carriers had not significantly different serum lipids as compared with "the lack of E4" genotype carriers.

We found no association between ApoE allele distribution and neurological outcome following stroke. However, ApoE epsilon 4-allele carriage was a risk factor for fatal outcome during 30-day period (OR=2.65, 95% CI 0.96-7.29, p=0.05).

**Conclusion** Genetic variation at the ApoE locus in Polish IS patient's population is a genetic factor that influences plasma lipid levels. However, ApoE genotype and plasma lipid levels do not correlate with stroke patient's neurological outcome. Apo E 4 allele carriage is associated with increased risk of death in the early phase after stroke.

#### P 2009

##### **Correlation of soluble Fas/APO-1 level in cerebrospinal fluid and lesion volume in acute stroke patients – preliminary report**

D. Petracic<sup>1</sup>, D. Mahovic Lakusic<sup>1</sup>, N. Zurak<sup>1</sup>, S. Loncaric<sup>2</sup>, M. Matesin<sup>2</sup>

<sup>1</sup>University Hospital Zagreb, Zagreb, CROATIA, <sup>2</sup>Faculty of Electronic Engineering and Computing, Zagreb, CROATIA

**Background and aim** Cerebral ischemia studies in animal models have indicated that apoptosis-programmed cell death, might be a contributor to neuronal death. The aim of this study

was to correlate the level of soluble (s) Fas/APO-1 (apoptosis suppressing protein) in CSF, with lesion volume in acute ischemic stroke patients.

**Methods** Six male patients (mean age 63±10 years) with first acute ischemic stroke, verified by clinical examination and CT scan were included in the study. Patients with history of severe infection, congestive heart failure, autoimmune and malignant disease were not included.

Soluble Fas/APO-1 level in CSF was determined by ELISA on day 3 of disease onset. Volume of ischemic lesions on CT scans (performed on the same day) was measured by own software. Statistical analysis was performed by Kendall's tau test.

**Results** The CSF levels of sFas/APO-1 in acute stroke patients of the observed group, ranged from 0 to 1.8 U/ml. The volume of ischemic lesions on CT scans, ranged from 0.21 to 47.72 ml. There was statistically significant correlation between CSF level of sFas/APO-1 and volume of ischemic lesions on CT scans in stroke patients (correlation coefficient 0.6; p=0.045).

**Conclusion** The preliminary results demonstrate correlation between CSF level of sFas/APO-1 and volume of ischemic lesions on CT scans, suggesting possible pathophysiological contribution of apoptosis in acute stroke patients.

#### P 2010

##### **Contralateral carotid occlusion in acute ischemic stroke influence on short-term outcome**

F. Corea, M. Paciaroni, G. Silvestrelli, S. Amici, V. Caso, P. Milia, L. Parnetti, V. Gallai

Stroke Unit, University of Perugia, ITALY

**Background** Concerning the relevance of an asymptomatic contralateral carotid artery occlusion (ACO) for the outcome of ischemic stroke patients few data are available. A decreased collateral flow and thrombotic or embolic events might lead to a worse outcome. The North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET) study reported in 5% of cases the presence of a contralateral occlusion.

**Methods** Object of the study were 758 patients suffering from acute ischemic stroke consecutively included in the Perugia hospital based Stroke Registry from 1st January 2000 to 31st December 2001. Demographic data, risk factors, medical history, characteristics of stroke, outcome according to the Rankin scale (RS), Barthel index (BI) and Scandinavian Stroke Scale (SSS) were recorded. Diagnosis of carotid occlusion was performed according to duplex ultrasound findings performed at admission.

**Results** Twelve (1.58%) ACO were detected. All ACO patients suffered from a PACI subtype of stroke, due to large artery disease and presented a lower Barthel score at admission (33 vs. 45). Patients having ACO were more likely to have a severe disability and neurological deficit at admission (SSS admission 31 vs. 32; RS admission 3.8 vs. 3.2) and discharge (SSS discharge 35 vs. 37; RS discharge 3 vs. 2.3). Bivariate analysis showed a significant association (p=0.03) between ACO and the presence of a more severe disability at discharge.

**Conclusion** In our experience ACO, prevalence is comparable to that shown in the highly selected population of the NASCET study. Patients with ACO seem to suffer from more severe strokes having poorer outcome.

P 2011

**Association of C-reactive protein and leukocyte count with carotid atherosclerosis**R. Kazmierski, W. Kozubski, J. Dorszewska,  
Z. Adamczewska-Goncerzewicz*Karol Marcinkowski University of Medical Sciences, Poznan,  
POLAND*

**Introduction** A large number of current epidemiological studies have reported on association between low-grade inflammation and atherosclerosis.

**Objective** The aim of this study was to assess how the inflammatory markers, such as C-reactive Protein (CRP), fibrinogen and leukocyte count were associated with carotid atherosclerosis, in comparison with biochemical parameters, like serum lipids, homocysteine, vitamin B12, B6 and folic acid serum levels, or parameters of peripheral blood cells, such as red cell count, mean corpuscular volume, haematocrit and platelet count.

**Method** 128 subjects including 54 stroke patients were investigated. The mentioned above parameters were measured in a standard hospital laboratory and additionally for homocysteine and vitamins with the use of high-performance liquid chromatography. Intima-media thickness (IMT) a measure for atherosclerosis of common and internal carotid arteries was measured with the use of high resolution B-mode ultrasonography.

**Results** We found a strong correlation between carotid IMT and leukocyte count ( $r=5.24$ ;  $P<0.001$ ), CRP ( $r=4.14$ ;  $P<0.001$ ), and in a less degree between IMT and fibrinogen level ( $r=3.06$ ;  $P=0.003$ ). Adverse correlation between IMT and high-density lipoproteins ( $r=-4.13$ ;  $P<0.001$ ) and positive correlation for triglycerides ( $r=3.49$ ;  $P<0.001$ ) and homocysteine ( $r=2.12$ ;  $P=0.036$ ) was found. For the rest of the assessed parameters we did not find significant correlation.

**Conclusion** The inflammatory markers like leukocyte count and CRP were strongly associated with carotid atherosclerosis. They could be easy, quick and relatively cheap to perform in any hospital laboratory.

P 2012

**Circadian variations in blood parameters of micro-circulation in patients with acute cerebral ischemic event**K. Akhvediani, T. Djandjgava, J. Burduladze, G. Lomidze,  
R. Shakarishvili, N. Tsakadze*Sarajishvili Institute of Neurology and Neurosurgery, Tbilisi,  
GEORGIA*

It is considered that circadian rhythms have an actual influence on the dynamics and pathogenesis of stroke occurrence, both in ischemic and hemorrhagic events, while affecting over their determiners such as blood pressure, parameters of microcirculation, blood fibrinolytic activity etc.

The goal of current study was to evaluate the tendency of formation of completed ischemic stroke during the nighttime in patients predicted with transient ischemic attacks (TIAs) in debut of the cerebral ischemic event.

We evaluated 20 patients with TIAs on admission. There were performed blood pressure monitoring, measurement of blood viscosity, haematocrit and erythrocyte aggregation index (EAI) in blood samples drawn by venepuncture on admission and during the night time (0, 2, 6 a.m.) at first in-hospital day. It was also picked up the time lag of ischemic attack with comparison of above-mentioned parameters.

We found that blood fibrinolytic activity was depressed and EAI was inverted during the nighttime at 65% and 88.2% of patients

respectively. All of those patients had a completed ischemic stroke clinically since next morning in consequence of TIAs in debut. Patients with TIAs without forthcoming stroke had ischemic events just at daytime and considerably lower rates of diurnal changes in blood microcirculation parameters.

Thus, we might conclude that severity of brain ischemic damage is affected by circadian variations in blood microcirculation parameters. The identification of periods of high risk for vascular events may have important practical implications.

P 2013

**Isolated unilateral anterior cerebral artery infarction: clinical and magnetic resonance (MRI) features in a series of 7 patients**

D. Ulbricht, R. J. Metz

*Centre Hospitalier de Luxembourg, Luxembourg,  
LUXEMBOURG*

**Introduction** Infarction of the anterior cerebral artery (ACA) accounts for about 1% of all territorial strokes. Despite some case series, most of the knowledge on isolated ACA-stroke is based on case reports.

**Methods** Our standard work-up for patients with acute ischemic stroke including MRI with diffusion-weighted imaging (DWI) was applied and MRI/DWI defined acute ACA-stroke. Patients with other acute or older significant lesions were excluded.

**Results** 7 consecutive patients were included. Mean age was 48 years (range 23–85); 4 were women, 3 men. Lesions were complete in 1 patient and incomplete in 6 with a predominance of the territory of branches of the pericallosal artery supplying the anterior cingulate gyrus (ACC). Lesion side was left in 6 and right in 1 patient. The presenting clinical signs were akinetic mutism (mostly transient), apathy, and vegetative trouble. Crural hemiparesis was only found in one case, the others had slight and transient hemiparesis of the proportional type. Involuntary movements were present in one patient. The aetiology did not differ significantly from other stroke types. Outcome in everyday life was generally good with 5 patients resuming their everyday activities.

**Discussion** In our series, the clinical presentation of ACA-stroke was mainly a neuropsychological or psychiatric one. This results from the definition by MRI permitting to visualize lesions, which usually escape detection by computed tomography. The diagnostic challenge consists in constant awareness of subtle neurological signs permitting a clinical diagnosis of a probably under recognized stroke syndrome.

P 2014

**Vascular endothelial growth factor in patients with large vessel versus small vessel ischemic stroke**S. M. A. Said, M. M. Hamdy, T. M. Mostafa, M. T. Afifi  
*Alexandria University, Alexandria, EGYPT*

**Objectives** We aimed at studying the role of vascular endothelial growth factor (VEGF) in small and large vessel ischemic strokes.

**Backgrounds** Growth factors may play different roles in the cerebral ischemic events. They may play role in the healing process and functional reorganization neurons during ischemia. They may also have neuroprotective properties after brain injury or ischemia.

**Designs and methods** VEGF was measured in the sera of 40 patients with acute ischemic stroke within one week of onset. Patients were divided into 2 groups; group I included 20 patients with large vessel diseases and group II included 20

patients with small vessel diseases. VEGF was also measured in the sera of 20 healthy subjects as a control group.

**Results** The mean serum levels of VEGF were significantly higher in groups I (mean± std.error; 7.29±1.23 ng/ml) and II (4.63±0.99 ng/ml) than in the control group (2.13±0.32ng/ml) ( $z=-3.61$ ,  $p<0.0001$  &  $z=-2.54$ ,  $p<0.05$ ). However, there was no statistically significant difference between the mean serum levels of VEGF in-group I & II ( $z=-1.72$ ,  $p>0.05$ ).

**Conclusions** Our results indicate that VEGF may have an important role in both large and small vessel ischemic strokes.

P 2015

#### Circadian blood pressure pattern and occurrence of lacunar infarct

A. Erdemoglu, F. Tan, A. VARLIBAS

Kirikkale University, Department of Neurology, Ankara, TURKEY

**Background** Although the occurrence of lacunar infarction is closely related to arterial hypertension, the possible pathogenetic role of circadian blood pressure (BP) changes is controversial. This study was designed to evaluate the relationship between circadian BP changes and occurrence of lacunar infarct in the respect of possible risk factors.

**Methods and Patients** Patients, older than 50 years old who were admitted to our clinic were evaluated to detect the circadian BP pattern, occurrence of lacunar infarct and other risk factors. Twenty-nine patients with lacunar infarct and 29 controls were included into the study consecutively between 2000–2002 years. Detailed information and neurological examination were done. Ambulatory 24-hour BP measurements, laboratory examinations and radiological studies were performed. Variation in systolic and diastolic BP was defined as the difference between night and daytime.

**Results** Patients with lacunar infarct were significantly older and showed more often a history of arterial hypertension ( $p:0.02$ ). Daytime and nighttime BP values were significantly greater than controls ( $p<0.01$ ). A reduced circadian BP variation due to increased nighttime values was found different from controls. In the logistic regression analysis, a reduced systolic circadian BP variation ( $p<0.01$ , OR: 15.1 95% CI, 4.2–54.5), age ( $p:0.03$  OR, 1.01; 95% CI, 1.01–1.19), history of hypertension ( $p:0.001$  OR, 4.84; 95% CI, 1.47–15.97) and night time systolic BP values ( $p<0.001$  OR, 1.11, 95% CI, 1.05–1.17) were found to be determinants of lacunar infarction.

**Conclusion** Reduced systolic circadian BP variation may be an important factor for the occurrence of lacunar infarction besides age and history of hypertension.

P 2016

#### Haemorrhagic cerebrovascular events and Marfan syndrome (MF)

G. Struga<sup>1</sup>, J. Kruja<sup>2</sup>

<sup>1</sup>Neurology–Neurosurgery, Tirana, ALBANIA, <sup>2</sup>Neurology, Tirana, ALBANIA

**Background** E.T a 29 years old, female recovered in Clinic of Neurology UHC of Tirana was diagnosed with cerebral arteriovenous malformation (AVM), other findings included: dolichostenomelia, dolichocephaly, arachnodactily, joint hypermotility, thinner retina, high arched and narrow palate, mitral valve prolapsed.

Clinical diagnosis performed by Genetics Clinic for this patient was Marfan syndrome, an autosomal dominant disorder of

connective tissue. According relations between symptomatic cerebral haemorrhage and Marfan syndrome was attempt to demonstrate.

**Methods** All the records of patients with intracerebral and subarachnoidal haemorrhage recovered in clinic of Neurology and Neurosurgery UHC of Tirana from January 1991–January 2002 were retrieved and observed for relation with MS. Total observed patients 547 (arteriovenous fistula 0.5, cavernoma 1%, angioma 3.10%, AVM 5.66%, aneurysm 13.34%).

**Results** Two patients with Marfan syndrome were recovered in Department of Neurology and Neurosurgery in this period. Only one patient with MS had symptomatic AVM. The other one was recovered for specific meningitis, unrelated with haemorrhagic cerebrovascular event.

**Conclusion** According to our results there does not exist a relation between a haemorrhagic cerebrovascular event and Marfan syndrome or vice versa.

P 2017

#### Effect of duration and type of diabetes mellitus on cerebral haemodynamics

M. Dikanovic

General Hospital “Dr. Josip Benchevic”, Slavonski Brod, CROATIA

The aim of the study was to assess whether duration and type of diabetes mellitus influences cerebral haemodynamics. Mean blood flow velocity (MBFV) /TCD measurement/ in the Willis circle of diabetics and control group of healthy, 100 subjects aged 48–67 years. Diabetics were divided according to duration (L.T.5 and G.E.5 years), type and therapy for type I (insulin) and type II (peroral antidiabetic, diet). Patients with pathologic TCD distributed had their MBFV slowed down and were considered suspect of stenosis. Forty diabetics had their MBFV slowed down. In the control group, it was recorded in 11% of subjects, and in the diabetics group for G.E.5 years in 50% of patients. Suspect arterial stenosis was recorded in 15% of diabetics, 21.43% of those who had diabetes for G.E.5 years, and in none (0%) in the control group. In the type I, slowed down MBFV was recorded in 50% of patients, in those with type II in 34.88%, and in those with type, II treated with diet in 29.41% of patients. Suspect arterial stenosis was recorded in 22.5% of patients with type I, 11.63% with type II on peroral antidiabetic therapy, and in 5.88% with type II diabetes on diet alone. Proportion tests ( $p$  L.T. 0.05) indicated the duration and type of diabetes to influence cerebral haemodynamics, so that the patients with type I and diabetes duration of G.T.5 years had a much higher probability to have suspect stenosis and markedly slowed down MBFV in the circle of Willis.

P 2018

#### Serum magnesium level in acute ischemic stroke

S. Demirkaya, K. Uluc, A. Aydin, Z. Odabasi, O. Vural  
GATA, Ankara, TURKEY

**Introduction** A neuroprotective effect of magnesium in stroke has also been hypothesized. We planned to investigate the relationship between the clinical severity of acute ischemic stroke, infarct volume and the blood total magnesium levels.

**Methods** One hundred fifteen patients (mean age 62.7±11.0, between 29–83 years old, 61 male and 54 female) with acute ischemic stroke admitted to our clinic respectively and thirty healthy, age and sex matched subjects as controls (mean age

60.5±8.8 between 32–75 years old, 17 male and 13 female) were enrolled to our study. In the first 24 hours of stroke, venous blood samples were collected for total magnesium level detection with atomic absorption method. Clinical evaluation was made by NIHSS in the first day of illness. We created 3 subgroups according to NIHSS scores as follows; Group 1: 0–9, Group 2: 10–19, Group 3: 20–42. We also created 3 subgroups according to the infarct diameter seen in CT on the day five as follows: Group 1: <1 cm, Group 2: 1–3 cm, Group 3: >3 cm.

**Results** Mean total magnesium level of the patients was 17.7±3.57 mg/ml and that of controls was 17.9±3.52 mg/ml. Comparison of the means between groups revealed no statistical significance. It has been found no correlation between total magnesium levels and either clinical severity of acute ischemic stroke or infarct diameter.

**Conclusions** We did not find any supportive neuroprotective effect of endogenous total magnesium level during acute ischemic stroke.

#### P 2019

##### Content of FAS-receptors in acute period of the stroke

M. M. Gerasimova, S. Medvedeva

Tver Medical Academy, Tver, RUSSIAN FEDERATION

Presently in pathogenesis of stroke is emphasized the role of mechanism of apoptosis that results in deferred neuron's death. In the focus of angiocerebral conflict along with accumulation of free radicals, deprivation of growth factors and inhibition of tissue antioxidant systems, immune inflammation with generation of antiinflammatory cytokines is of great importance. Evolving of cytokine cascade is accompanied by influx of lymphocyte cells in zone of damaged brain tissue and by expression of leukocyte adhesive complex. All this induces Fas-receptors, which serve as marker SD95 and result in hyper expression in conditions of apoptosis of neural cells.

The aim of study was to learn the content of Fas-receptors (SD95) during acute period of stroke in conditions of arterial hypertension.

In clinical conditions, 17 patients were investigated (10 female and 7 male). Their age varied from 43 to 77 years. Mean age – 63.4 years. 12 patients had ischemic and 5 hemorrhagic stroke. According to Glasgow scale, loss of consciousness of severe grade showed 8 (summary index – 6.75±1.28), middle grade – 7(10.3±0.95), mild grade – 2(14.5±0.5).

The study showed increasing number of lymphocytes in blood, which were typified by Fas-receptors that was equal to 19, 6±7.4%. Its level correlated with severity of stroke. In cases of the stroke of severe grade level of monoclonal antibodies was 26.4±3.0%, in cases of middle grade – 15.4±2.1%, in mild grade – 7±1.4% (p<0.001). Autoimmune process in brain results in neuron's death in the form of apoptosis, degrees of which correlates with stroke severity grade.

#### P 2020

##### Acute vascular spinal disturbances in Scheuermann disease

D. G. Gherman<sup>1</sup>, S. M. Plesca<sup>2</sup>, V. S. Lisnic<sup>1</sup>, M. M. Sangheli<sup>1</sup>

<sup>1</sup>Medical State University, Chisinau, REPUBLIC OF MOLDOVA, <sup>2</sup>Center of Neurology & Neurosurgery, Chisinau, REPUBLIC OF MOLDOVA

**Objective** The neurological complications within Scheuermann disease (SD) are observed in 13–15% cases. The goal of the study was to establish the role of the degenerative vertebral process within SD in evolution of spinal stroke.

**Material and methods** 8 patients were examined (2 females and 6 males), aged from 19 to 46 years with spinal stroke on the baseline of existing SD. The patients underwent neuroimaging examinations by means of routine spondilography and spine magnetic resonance imaging (MRI).

**Results** In all cases stroke developed in the supply area of A. Adamkiewicz. The medullar vascular disturbances manifested as syndrome of complete transverse medullar lesion. The patients experienced an acute onset within minutes or several hours manifested by flask paraplegia, conductive sensory loss, and central sphincter disturbances. Radiological modifications presented as excessive thoracic kyphosis with apex localization at the Th9–Th10 level – in 6 cases, Th5–Th7 – in 2 cases, osteoporosis of the cuneiform vertebrae – in all the examined cases, reduced intervertebral disks height, associated with Schmorl hernias – in 6 patients. MRI revealed signs specific for medullar ischemia. In 2 cases a marked tumefaction with hyper intensity in T2w regime at the Th5–Th7 levels were established, with extension from Th9 to Th11 levels – in 5 cases and to Th12–L1 – in one case. Spinal channel stenosis at the thoracic level was detected in 4 patients.

**Conclusion** The degenerative spinal modifications within SD should be considered as etiological factor in spinal stroke in young persons.

#### P 2021

##### Relation between erythrocyte deformability and blood flow velocity in cerebral arteries in heavy alcohol drinkers in acute stage and after withdrawal

Z. Gdovinova

University P. J. Safarik, Faculty of Medicine, Kosice, SLOVAKIA

**Introduction** Significantly, decreased blood flow velocity in cerebral arteries as well as decreased erythrocyte deformability in heavy alcohol drinkers was found (Gdovinova et al., 2002). The aim of the study was to determine if there is correlation between them.

**Methods** The study comprised of 47 patients, heavy alcohol drinkers (mean age 47 years). Mean flow velocity ( $V_{\text{mean}}$ ) was determined by a 2 MHz pulsed Doppler probe. Erythrocyte membrane biophysical properties were estimated using the method of cation-osmotic haemolysis (COH) developed by Nicak and Mojzis (1992). The results were compared with results in 20 healthy volunteers of the same age. Differences between these two groups were tested with Student's t-test. Relation among blood flow velocity and cation-osmotic haemolysis (COH) was analysed by methods of regressive and correlative analysis.

**Results**  $V_{\text{mean}}$  was significantly decreased in all cerebral arteries.  $V_{\text{mean}}$  in MCA was 52±/–8.74 cm/s vs. 59.2±/–9.1 cm/s (p<0.001). COH was significantly decreased in the medium of low and high ionic strength (15.4 mmol/l NaCl) resp. (123.2–154 mmol/l NaCl) (p<0.01). Linear correlation between COH and  $V_{\text{mean}}$  was found by correlative analysis ( $V_{\text{mean}}=0.226 \cdot \text{COH}+40.55$ , correlation coefficient  $R=-0.56$ , p<0.01). After withdrawal,  $V_{\text{mean}}$  was increased while COH was not significantly changed.

**Conclusion** There is linear relation between  $V_{\text{mean}}$  in cerebral arteries and cation-osmotic haemolysis in acute stage in heavy alcohol drinkers. In conclusion, decreased ED could be the reason of decreased  $V_{\text{mean}}$ , which is the risk factor of stroke.

P 2022

#### Tinnitus and cerebrovascular disease

N. Runjic

*SUVAG, Zagreb, CROATIA*

**Introduction** The auditory and vestibular systems share the same end organ and cranial nerve, yet vestibular signs and symptoms are common with cerebrovascular disease, whereas hearing disturbances are much less frequent. The most hemispheric lesions produce subtle hearing dysfunctions that can only be detected with sophisticated psychoacoustics and electrophysiological testing. The aim of this study was to evaluate the occurrence of risk factors for cerebrovascular disease in patients suffering from cochlear tinnitus.

**Methods** We tested 48 persons with subjective, cochlear tinnitus (patients), 35 women and 13 men, aged 30–65 years. Our results were compared to the control group of 50 persons without tinnitus, 36 women and 14 men, aged 28–66 years.

All subjects had a complete neurootologic examination with medical history, standard blood testing, audiometry and vestibular testing. Colour Doppler Flow Imaging of carotid and vertebral arteries and Transcranial Doppler were also performed.

**Results** The risk factors for cerebrovascular disease, hypertension, diabetes, hyperlipidemia and smoking were significantly more often in patients than controls. Patients with tinnitus had significantly more often the vertebrobasilar insufficiency evaluating by Transcranial Doppler.

**Conclusion** These results show that identification of risk factors for cerebrovascular disease may lead to prevention or effective treatment of cochlear tinnitus.

#### References

1. Jastreboff PJ, Hazell JWP (1993). A neurophysiological approach to tinnitus: Clinical implications. *Brit Audiol* 27:1–11.
2. Vernon JA (1998). *Tinnitus*. Boston: Allyn and Bacon.
3. Hausler R, Levine RA (2000). Auditory dysfunction in stroke. *Acta Otolaryngol* 120:689–703.

P 2023

#### Asymptomatic carotid stenosis in patients who have claudication

S. Toncevic, R. Pavlovic, G. Toncevic

*Clinical Hospital Center, Kragujevac, YUGOSLAVIA*

**Introduction** Atherosclerosis is a generalized and progressive disease. Patients with symptomatic peripheral vascular disease often have symptomatic or asymptomatic disease elsewhere in the vascular system.

The aims of this study are to investigate the prevalence of asymptomatic carotid stenosis in patients who have claudication as the mildest form of peripheral vascular disease and to identify high/risk groups among these patients.

**Methods** Screening for internal carotid artery using duplex colour flow scan were performed on 102 patients with claudication and with no history of cerebrovascular symptoms or prior carotid endarterectomy. Patients with carotid stenosis were divided in four groups: mild, moderate and severe carotid stenosis, and total occlusion on at least one side. Associated atherosclerotic risk factor were assessed (patient age, sex, diabetes, hypertension, smoking history and lipid levels).

**Results** The prevalence of previously unknown mild carotid stenosis was 52.94%. The prevalence of moderate carotid stenosis was 33.33%. In 13.72% of patients, carotid examination produced severe carotid stenosis. There was no patient with total occlusion. Asymptomatic carotid stenosis was found to significantly correlate with male sex ( $p=0.011$ ), smoking history ( $p=0.000$ ) and advanced age ( $p=0.000$ ).

**Conclusion** Routine duplex screening has benefit in all patients who seek medical attention with claudication to detect asymptomatic high-grade carotid stenosis.

P 2024

#### Epileptic seizures as a manifestation of stroke

D. Kuljic-Obradovic, S. Atic, M. Savic, M. Jovanovic

*Hospital for Cerebrovascular Diseases "St. Sava", Belgrade, YUGOSLAVIA*

**Introduction** Epidemic studies have been accomplished showing a wide variation in frequency of epileptic seizures in different types of stroke.

**Objective** The objective was to compare the frequency of epileptic seizures in different type of stroke.

**Methods** We studied all the stroke patients admitted to our Hospital from January 2002 to April 2002. The patients were studied using a standard protocol including at least one CT scan within 7 days of the stroke and EEG.

**Results** 1050 patients with stroke were attended, 494 female and 556 male, age range 32 to 91. Among these stroke patients, 87 had experienced first epileptic seizures in onset of stroke. The following results of frequency of epileptic seizures were provided: in patients with single ischemia 27, with multiple ischemic brain lesions 29, with hemorrhagic ischemia 1, with SAH 2, with haemorrhage 5, in haemorrhage with seepage into the ventricular system 5 patients and in patients with cerebral atrophy 18. Frequency rates were established for different types of seizures as follows: 15 patients had simple focal, 12 complex focal, 13 secondarily generalized and 47 generalized seizures.

**Conclusions** Among the patients with stroke in our study the frequency of epileptic seizures was 8.3% with the highest frequency in the patients with cerebral atrophy (23.4%). The frequency was nearly similar in the ischemic (7.3%) and hemorrhagic (6.2%) stroke. The majority of the seizures that occur de novo in stroke patients were focal in onset with or without secondary generalization.

P 2025

#### Serum level of soluble thrombomodulin in acute ischemic stroke

E. Nomura<sup>1</sup>, T. Kohriyama<sup>2</sup>, H. Kajikawa<sup>3</sup>, S. Nakamura<sup>1</sup>, M. Matsumoto<sup>2</sup>

<sup>1</sup>Department of Neurology, Suiseikai Kajikawa Hospital, Hiroshima, JAPAN, <sup>2</sup>Department of Clinical Neuroscience and Therapeutics, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, JAPAN, <sup>3</sup>Department of Neurosurgery, Suiseikai Kajikawa Hospital, Hiroshima, JAPAN

**Background and Purpose** The purpose of the present study was 1) to investigate sequential changes in soluble thrombomodulin (sTM) concentrations following acute ischemic stroke, 2) to reveal differences between large and small vessel diseases, and 3) to correlate sTM concentrations with the severity of stroke and functional outcome.

**Methods** Seventy-seven patients with acute ischemic stroke admitted within 48 hours from the onset were enrolled. Blood examinations were carried out at admission and 1 month after admission. We tested the Japan Stroke Scale at admission to evaluate the severity and the Functional Independence Measure (FIM) to evaluate the functional outcome of the patients 1 month after admission.

**Results** Serial examination revealed that sTM concentrations 1 month after the admission (median [25th–75th percentile], 3.5 ng/ml [3.0–4.6]) were significantly higher than those at admission (3.3 ng/ml [2.8–4.2]). sTM concentrations at admission were significantly lower in large vessel (3.1 ng/ml [2.7–3.5]) disease than in small vessel disease (3.6 ng/ml [3.1–4.6]), and showed significant inverse association with severity of stroke, and tended to be lower in patients with poor outcome (scoring <100 on FIM) than good outcome (scoring  $\geq$ 100 on FIM).

**Conclusions** Although sTM concentrations serve as useful markers for endothelial cell damage, surprisingly, they are rather decreased in acute ischemic stroke patients in proportion to the severity. The mechanism of this unique result is still uncertain, however, lower sTM concentrations may play some important role in disease progression or in the occurrence of vascular events following acute ischemic stroke.

#### P 2026

##### **Cholesterol levels in patients with transient global amnesia**

S. Papapetropoulos, P. Talelli, G. Katsoulas, E. Chroni, J. Ellul, C. Paschalis

*University of Patras, Department of Neurology, Patras, GREECE*

Transient global amnesia (TGA) is a well-defined syndrome of unknown aetiology. Vascular risk factors epilepsy and migraine have been implicated. We studied the cholesterol levels, between other risk factors, in a group of consecutive TGA patients admitted in our hospital. These levels were compared with those of patients admitted with minor stroke and of healthy controls both matched for age and sex.

23 patients with TGA [mean age 61.2 ( $\pm$ 6.8), females 12 (52%)] were included in the study. 8 (35%) had arterial hypertension, 2 (9%) diabetes mellitus, 2 (9%) ischaemic heart disease. No relevant lesion was found in the brain imaging. EEG showed non-specific abnormalities in 4 (18%) patients. Carotid ultrasound showed mild atheromatosis in 5 (22%) patients, but significant stenosis only in one. Two patients had history of migraine.

In the group of patients with TGA the mean cholesterol level was 263.1 ( $\pm$ 47.4) compared with 236.9 ( $\pm$ 55.2) in the stroke group ( $p=0.055$ ) and 209.8 ( $\pm$ 30.8) in controls ( $p<0.0001$ ). However, female patients with TGA had significantly higher cholesterol levels compared with both stroke patients and healthy controls ( $p=0.049$  and  $p=0.002$  respectively). No statistical difference was found in the comparison of male TGA patients with the stroke patients.

Cholesterol levels in TGA patients are significantly higher compared with healthy controls, and tended to be higher compared with stroke patients matched for age and sex. Vascular risk factors may play an important role in the etiopathogenetic mechanism of transient global amnesia and are currently studied in a larger sample.

#### P 2027

##### **Posterior cerebral artery infarction, aetiology, radiological findings and clinical outcome**

E. Vasiliadou<sup>1</sup>, K. Spengos<sup>2</sup>, P. Siemou<sup>1</sup>, G. Tsivgoulis<sup>2</sup>, V. Katsitopoulou<sup>1</sup>, P. Konstantopoulou<sup>3</sup>, K. N. Vemmos<sup>3</sup>

<sup>1</sup>*Dept of Radiology, Alexandra Hospital, Athens, GREECE,*

<sup>2</sup>*Dept of Neurology, Medical School, University of Athens, Athens, GREECE,*

<sup>3</sup>*Dept of Clinical Therapeutics, Medical School, University of Athens, Athens, GREECE*

**Aim** Goal of our study was the evaluation of stroke aetiology, radiological findings, and outcome in patients with acute ischemic stroke involving the Posterior Cerebral Artery (PCA).

**Subjects and Methods** 1520 first-ever stroke patients were admitted to our hospital. A CT-scan was initially performed, while 58% of the patients had a second CT- or MRI-Scan during hospitalisation. Stroke was classified based on etiopathogenic mechanisms. Follow-up ranged from 1 month to 6 years. Survival was determined using Kaplan-Meier estimates.

**Results** Infarction in the vertebrobasilar territory was diagnosed in 327 patients (21.5%). Involvement of the PCA was identified in 100 cases (6.58%). 54 of them presented ischemic lesions restricted in the PCA-territory, while the rest (46%) showed also other single or multiple ischemic lesions (thalamic, cerebellar, pontine). In 70% of the cases, the lesion was visualized within the first 24 hours. Hemorrhagic transformation was noted in 21%. Cardioembolic stroke in the posterior circulation was the most common diagnosis (51%), followed by stroke of unknown cause (37%). Early mortality rate (1 month) was significantly lower (11%) among patients with isolated PCA-infarction than in patients with PCA-infarction and other ischemic lesions. Accumulative mortality after 47.2 months (median value) showed similar differences (40% vs. 56%).

**Conclusions** PCA involvement is manifest in 1/3 of all posterior infarcts and is mostly visible within 24 hours. Cardioembolism is the major cause of stroke in the posterior territory. Patients with PCA and other lesions have a significantly higher early and late mortality rate than patients with isolated PCA infarction.

#### P 2028

##### **Association between blood pressure changes and outcome in acute stroke**

V. Vargek Solter, M. Bosnar Puretic, M. Bosnjak Pasic,

T. Breitenfeld, V. Demarin

*Neurology Department University Hospital "Sestre milosrdnice", Zagreb, CROATIA*

**Introduction** The aim of this study is to establish the association between blood pressure (BP) changes and outcome in acute stroke (ischemic (ISH) and intracerebral haemorrhage (ICH)).

**Methods** This prospective study included patients with severe stroke (ISH and ICH) admitted to intensive care unit within 6 hours after stroke onset. BP was measured every 2 hours during first 72 hours after stroke onset. Stroke severity and outcome was assessed using Scandinavian Stroke Scale at the time of admission (SSSa) and discharge (SSSd) from hospital.

**Results** This study included 114 stroke patients (85 ISH and 29 ICH), mean age 73.1 $\pm$ 12.9 years.

Mean systolic BP at admission in ISH was 157 $\pm$ 16.8mmHg, SSSa $>$ 16 had higher values. In ICH patients BP at admission was 163.4 $\pm$ 19.3 mmHg, higher values were found in patients with SSSa $<$ 15.



Systolic BP during first 72 hours was higher in ICH than in ISH patients (162.6mmHg; 146.5mmHg, respectively). BP during first 72 hours in ICH group was continuously higher in patients who died and with SSSd<15 than in survivors with SSSd>16. Better outcome was observed in ISH patients with moderate higher BP during first 72 than in patients with lower BP. SSSa was higher in ISH than in ICH patients. In ICH group 29% of patients died, but survivors had better SSSd than survivors in ISH group.

**Conclusions** BP is important factor in prognosis of stroke course and outcome. Moderate higher BP in ISH is associated with better outcome. In ICH patients, the problem was serious hypertension, often resistant to therapy.

#### P 2029

##### **Blood glucose and outcome in acute ischemic stroke: Differences between diabetic and non-diabetic patients**

M. Bosnar Puretic, V. Vargek Solter, M. Bosnjak Pasic, H. Hecimovic, V. Demarin

*Neurology Department University Hospital "Sestre milosrdnice", Zagreb, CROATIA*

**Introduction** Influence of hyperglycaemia on stroke outcome is known. We wanted to investigate the influence of blood glucose level on admission on stroke severity and outcome in diabetic (DM) and non-diabetic patients (non-DM).

**Methods** Prospective study included 106 patients with ischemic stroke admitted to intensive care within 6 hours after stroke onset. In all patients blood glucose level at admission and twice a day during first 72 hours after stroke onset was measured (mmol/l). Stroke severity on admission was assessed using Scandinavian stroke scale (SSSa) and outcome in survivors using Barthel index (BI).

**Results** Out of 106 patients 28 had diabetes. Mean glucose at admission was 9.3 mmol/l in DM and 6.9 mmol/l in non-DM. Mean SSSa didn't significantly differ between DM and non-DM. DM with glucose at admission >9.1 had significantly lower SSSa (mean=17.5) than DM with glucose <9.1 (mean=20). Similar was in non-DM group: in patients with glucose >9.1 mean SSSa was 20.4 and with glucose <9.1 SSSa was 13.3. During first 24–48 hours in DM group significant rise of glucose occurred. DM had worse outcome than non-DM regardless of glucose on admission. But in non-DM significant difference in outcome regarding glucose on admission was present: in patients with glucose <9.1 mean BI was 38.8 and with glucose >9.1 BI was 26.2.

**Conclusions** We found no certain evidences of diabetes mellitus influence on stroke severity, but it is evident that it is associated with slower recovery and poor outcome, especially if glucose level at admission is higher.

#### P 2030

##### **Changes of body temperature during first 72 hours and outcome of ischemic stroke and intracerebral haemorrhage**

M. Bosnar Puretic, V. Vargek Solter, T. Breitenfeld, V. Lovric, V. Demarin

*Neurology Department University Hospital "Sestre milosrdnice", Zagreb, CROATIA*

**Introduction** Experimental and clinical studies showed that hyperthermia early after stroke onset causes further brain damage and poor outcome. Some studies showed relation of low

temperature on admission and stroke severity. The aim of our study was to follow up the body temperature changes early after stroke onset and to compare the differences between patients with good and poor outcome.

**Methods** We enrolled stroke patients (ischemic stroke (ISH) and intracerebral haemorrhage (ICH)) admitted to intensive care unit within 6 hours after stroke onset. In all patients CT scan was done. Stroke severity on admission was assessed using Scandinavian stroke scale, and outcome using Barthel index (BI) approximately after 15–21 days. Temperature was measured with tympanic thermometers every two hours during first 72 hours after stroke onset.

**Results** In ICH patients with better outcome (BI>60) temperature on admission was lower than in patients with BI<60 or dead. Rapid rise of temperature occurred earlier in patients with BI<60 (after 12–18h) and dead (6–12h). In patients with BI>60 rise in temperature occurred after 48 hours, potentially of infectious origin. In ISH patients, better outcome had patients with higher temperature at admission. In these patients (BI>60) during first 72 hours, there were no significant changes in temperature. Patients with BI<60 and dead had lower temperature at admission, with early (6–12h) and rapid rise continuously during 72 hours, with low response to antipyretic drugs.

**Conclusions** Early rise of temperature can be related to poor outcome of stroke patients.

#### P 2031

##### **Clinical parameters influencing the survival after stroke**

L. Csiba<sup>1</sup>, J. Szász<sup>2</sup>, L. Kardos<sup>3</sup>, A. Lengyel<sup>1</sup>, D. Bereczki<sup>1</sup>  
*<sup>1</sup>Debrecen University, Debrecen, HUNGARY, <sup>2</sup>Targu Mures University, Targu Mures, ROMANIA, <sup>3</sup>Public Health School, Debrecen, HUNGARY*

**Background** Trends of BP (1st week) and admission, glucose, blood cells, and urea values were analysed.

**Methods** Clinical data of ischemic stroke patients were retrospectively analysed. Follow-up times were counted from diagnosis to death or censored upon discharge. Other data included age, sex, daily blood pressure readings, laboratory results, pharmaceutical therapy, and laterality of stroke. Daily blood pressure readings were summarized in terms of intercept and slope of linear regression line against time. Univariate Cox regression models were fitted for all possible explanatory variables in their original and quadratic forms where applicable. Results were expressed as hazard ratios associated with clinically relevant changes. Multivariate Cox regression models were fitted using blood pressure and the subset of other variables either with significant hazard ratios or considerable influence on other coefficients.

**Results** 81 patients died before discharge and 84 survived. Univariate models revealed significantly worse survival associated with being male, having higher white blood cells, urea, glucose, and lower cholesterol. A minimum of the hazard ratio was observed at the potassium level of 4.8 mmol/l. The daily maximum systolic BP showed a quadratic association with survival in terms of both intercept and slope and also an interaction between the two, therefore it was chosen to be used in the final multivariate model. Factors with substantiated reason to be included in the model were sex, age, white blood cell count, and potassium. Being male, older, having a higher white blood count and a lower serum potassium level were associated with worse survival.

## P 2032

**Moyamoya disease**

C. Reis, P. Abreu, F. Simões, C. Neves, C. Pontes  
*Department of Nervous System Diseases, Hospital S.João,  
 Porto, PORTUGAL*

**Introduction** Moyamoya is an uncommon cause of ischemic and hemorrhagic stroke in children and young adults, most prevalent in Asia. There is a progressive obliteration of Willis' circle major arteries, which are replaced by a fine meshwork of small vessels resembling a "puff of smoke", source of the name Moyamoya. Diagnostic evaluation includes cerebral magnetic resonance imaging (MRI), angiography and single photon emission computed tomography (SPECT). Treatment resembles the normal management of stroke with the addition of possible revascularisation procedures. Steroids have been successfully used in a few cases of Moyamoya disease with extrapyramidal symptomatology.

**Methods** We report a case of a 19 years old woman with a previous history of oral contraceptives intake since February 1999 and reversible right hemiparesis (RIND) in August 1999. On January 2002, the patient was hospitalised due to headache and progressive bradykinesia and bradyphrenia within the last year, with increased severity two weeks before admission, along with bilateral loss of vision, dysarthria and motor dysphasia. During hospitalisation, the patient developed global aphasia and right hemiparesis.

**Results** Cerebral MRI showed bilateral multiple lesions, in gray and white matter, in different stages. Angiography showed bilateral thrombosis of medial cerebral artery and multiple collateral small vessels were seen resembling a puff of smoke. Left cortical hypoperfusion, in temporo-parieto-occipital regions, was seen in cerebral SPECT.

**Conclusion** Treatment with acetylsalicylic acid and dexamethasone led to partial clinical improvement. We report this case that clinically and in imaging studies behave like Moyamoya disease due to its rareness and atypical presentation with extrapyramidal symptomatology.

## P 2033

**Subcortical ischemia, the gentle emerging outsider**

C. Ramos-Estebanez<sup>1</sup>, H. Alonso<sup>1</sup>, R. Munoz-Arrondo<sup>2</sup>, I. Moral-Arce<sup>1</sup>, A. Gonzalez-Mandly<sup>3</sup>, J.L. Hernandez<sup>1</sup>, P. Matorra<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, <sup>2</sup>Department of Neurology,

<sup>3</sup>Department of Radiology, Marques de Valdecilla University Hospital, Santander, SPAIN

**Purpose** To describe subcortical vascular dementia (SVaD) regarding clinical presentation, risk factors, and prognosis.

**Methods** 185 vascular demented subjects studied during the last 7 years are divided into SVaD (n=85), and non-SVaD (n=100) groups. The latter met the ADDTC criteria, while SDaV patients were diagnosed of lacunar state (n=33), or met Bennet's criteria for Binswanger's disease (n=52). Hemorrhagic strokes, and mixed dementias are excluded. Univariate and multivariate analysis are performed.

**Results** Transient ischemic attacks appear before diagnosis of dementia in SVaD, while stroke associates with non-SDaV patients (p<0.05). There is a significantly greater prevalence of hypertension and dyslipimiamia in the SDaV patients. Rankin's modified scores are more benign in SDaV subjects at diagnosis. Non-SDaV patients present with <1 month of ischemic data before diagnosis of dementia (p<0.05), whereas SDaV show 1 to 24 months of progression before diagnosis (p<0.05). The

equation for the model is:  $Z=3.7*(\text{Rankin score}=1 \text{ at diagnosis})+3.4*(\text{Rankin score}=2 \text{ at diagnosis})-3.0*(\text{Rankin score} \geq 3 \text{ at diagnosis})-1.7*(\text{ischemic stroke prior to diagnosis})-2.2*(\text{clinical data during } <1 \text{ month before diagnosis})-2.8$ .

**Conclusions** SDaV shows an increasing incidence in our area. Transient ischemic attacks, dyslipimiamia, and hypertension feature SDaV. SDaV have milder Rankin scores at discharge. Ischemic strokes before diagnosis are more frequent in non-SDaV.

## P 2034

**Epileptic seizures after stroke**

B. Glawar<sup>1</sup>, J. Ferrari<sup>2</sup>, M. Zartl<sup>1</sup>, A. Gornik<sup>1</sup>, W. Lalouschek<sup>2</sup>, B. Mamoli<sup>1</sup>

<sup>1</sup>Neurologisches KH Rosenhügel, Wien, AUSTRIA, <sup>2</sup>Abt. für Klinische Neurologie der Universitätsklinik für Neurologie, Wien, AUSTRIA

The reported incidence of seizures after stroke varies from 4 to 15%, the incidence of epilepsy after stroke ranges from 4 to 9%. We present the first results of the Vienna Stroke Registry on the occurrence of single epileptic seizures and epilepsy in patients after ischemic or hemorrhagic stroke or TIA.

From 1969, 82 patients had one or more epileptic seizures in an observation period of three months after the event. This is an incidence of 4.2%. 55 patients had their first seizure within 24 hours. In another 22 patients, the first seizure occurred within 14 days after the stroke or TIA. This means that in total, 94% of the 82 patients had "early onset seizures". 5 patients had late onset seizures occurring at least 14 days after the event.

Out of these 82 patients, 67% had partial seizures with and without secondary generalisation and in 33% phenomenologically primarily generalised tonic-clonic seizures were documented.

In a multivariate analysis, patients with initially severe deficits had a significantly higher risk of suffering from seizures.

More than one epileptic seizure occurred in 12 of the patients, which is an incidence of 0.6% for epilepsy after stroke from the total pool of patients studied.

Compared with the literature the incidence of epilepsy occurring in our patients after stroke is too low. With follow-ups after one and two years, we should be able to give more detailed results concerning the incidence of late onset seizures and vascular epilepsy.

## P 2035

**Disorders of cardiac rhythm in stroke**

B. Z. Jovanovic, A. Pavlovic, J. Zidverc Trajkovic, M. Mijailovic, N. Sternic, S. V. Kostic  
*Institute of Neurology KCS, Belgrade, YUGOSLAVIA*

Some cardiac rhythm disorders may be risk factors for stroke. Atrial fibrillation is a good established risk factor for thromboembolic stroke. We examined all types of rhythm disorders and their potential importance for stroke appearance.

We investigated 92 patients (average 60,5 years, 49 men, 43 women) with stroke (that was proven by MRI or CT of the brain). They had been known as patients with cardiac dysrhythmias earlier. From them, 84.78% of patients had ischemic and 15.21% hemorrhagic stroke. We examined types and frequency of cardiac dysrhythmia and correlated them with control group (75 healthy persons).

There were 39.13% patients with dysrhythmias in investigation groups, and 9.33% in control groups. Cardiac rhythm disorders were statistically important risk factor of ischemic insults

( $\chi^2=24.25$ ,  $p<0.001$ ) and were not important for haemorrhages ( $\chi^2=3.281$ ,  $p>0.05$ ). The most important were: atrial flutter or fibrillation, absolute arrhythmia ( $\chi^2=13.86$ ,  $p<0.001$ ); the similar importance was for paroxysmal tachycardia and third degree cardiac block. We didn't find importance for tachycardia until 150/min, extrasystols and block of I or II degree. The mechanisms of atrial fibrillation (and the similar cardiac disorders) were in thromboembolism of cerebral arteries, but high degree cardiac block-III had hemodynamic mechanism. We concluded that cardiac dysrhythmias (atrial flutter or fibrillation, absolute arrhythmia, paroxysmal tachycardia and high degree cardiac block) were risk factors for ischemic stroke.

P 2036

**Clinical and immune changes in the hemorrhagic stroke**

M. M. Gerasimova, G. N. Zhdanov, J. V. Antipina  
Tver Medical Academy, Tver, RUSSIAN FEDERATION

P 2037

**Correlation of transient ischemic attacks symptoms with atrial fibrillation occurrence**

E. Apanel, A. Mastysin  
Research Institute of Neurology, Neurosurgery and  
Physiotherapy, Minsk, BELARUS

P 2038

**The sequelae of stroke aphasia**

S. Kory Calomfirescu<sup>1</sup>, A. M. Mos<sup>2</sup>, M. Kory Mercea<sup>1</sup>,  
S. Ioncu Demea<sup>3</sup>  
<sup>1</sup>Univ. of Medicine, Cluj-Napoca, ROMANIA, <sup>2</sup>Univ. of  
Medicine, Oradea, ROMANIA, <sup>3</sup>Univ. of Medicine, Arad,  
ROMANIA

P 2039

**Wallenberg syndrome masking with cerebellar hemispheric infarction**

G. Ivkic<sup>1</sup>, Z. Mubrin<sup>2</sup>, J. Papa<sup>2</sup>  
<sup>1</sup>Croatian Institute for Brain Research, Zagreb, CROATIA,  
<sup>2</sup>Zagreb University Hospital Centre, Zagreb, CROATIA

P 2040

**The lateral sinus thrombosis in woman with prothrombin gene variant (G20210A) and antiphospholipid antibody syndrome; a case report**

M. Mijajlovic<sup>1</sup>, J. Zidverc-Trajkovic<sup>1</sup>, A. M. Pavlovic<sup>1</sup>,  
Z. Jovanovic<sup>1</sup>, D. Kozic<sup>2</sup>, P. Miljic<sup>3</sup>, M. Kovac<sup>4</sup>, N. Sternic<sup>1</sup>,  
V. S. Kostic<sup>1</sup>  
<sup>1</sup>Institute of Neurology, Belgrade, YUGOSLAVIA, <sup>2</sup>Institute of  
Magnetic Resonant Imaging, Sremska Kamenica,  
YUGOSLAVIA, <sup>3</sup>Institute of Haematology, Belgrade,  
YUGOSLAVIA, <sup>4</sup>Institute of Blood Transfusion of Serbia,  
Belgrade, YUGOSLAVIA

P 2041

**Diastolic arterial blood pressure at venous discirculatory encephalopathy**

V. V. Mashin, T. Z. Biktimiriv, G. M. Doroshenko  
Ulyanovsk State University, Ulyanovsk, RUSSIAN  
FEDERATION

**Movement disorders 1**

P 2042

**Effect of endocannabinoids on [<sup>3</sup>H]-gaba uptake in rat globus pallidus – relevance to Parkinson's disease**

K. Venderova<sup>1</sup>, T. M. Brown<sup>2</sup>, J. M. Brotchie<sup>2</sup>, E. Ruzicka<sup>3</sup>,  
P. Visnovsky<sup>1</sup>  
<sup>1</sup>Faculty of Pharmacy, Charles University, Hradec Kralove,  
CZECH REPUBLIC, <sup>2</sup>School of Biological Sciences,  
University of Manchester, Manchester, UNITED KINGDOM,  
<sup>3</sup>1st Medical Faculty, Charles University, Prague, CZECH  
REPUBLIC

Globus pallidus is one of the major constituent nuclei of the basal ganglia. Within the globus pallidus, there is a high density of CB<sub>1</sub> cannabinoid receptors and high levels of endocannabinoids. To date, three endocannabinoids have been identified: anandamide 2-arachidonyl glycerol (2-AG), and noladin ether. In the globus pallidus, CB<sub>1</sub> receptors are localized presynaptically on GABAergic neurons. Activation of CB<sub>1</sub> receptors is believed to result in inhibition of GABA release. We focused on the influence of endocannabinoids on GABA uptake in freshly isolated rat globus pallidus slices. Following incubation with 2-AG (1 microM and 3 microM), we observed a 40%, and 30% increase respectively in [<sup>3</sup>H]-GABA uptake ( $p<0.05$ , one-way ANOVA and Turkey's post test). When incubated with noladin ether (1 microM), an increase of 57% was observed ( $p<0.001$ ). The effects of 2-AG were reversed by the CB<sub>1</sub> receptor antagonist AM 251 (1 microM), showing this mechanism is likely to be CB<sub>1</sub> receptor-mediated ( $p<0.05$ ). In contrast, neither anandamide (0.1–10 microM) nor the synthetic CB<sub>1</sub> receptor agonist WIN 55,212-2 (1–100 microM) had significant effect on GABA uptake compared to the vehicle. Experiments in animal models of Parkinson's disease suggest that the cannabinergic system plays a role in the pathophysiology of Parkinson's disease, our results might help to explain the mechanism.

Supported by Charter 77 Foundation and FRVS Grant 2223/02.

P 2043

**Sumanriole does not increase the incidence of somnolence as measured by the ESS**

K. A. Selzer, K. Chapman, S. L. Simpson, M. Wang  
Pharmacia Corporation, Kalamazoo, MI, USA

**Introduction** Sumanriole is a new dopamine agonist specific for the D<sub>2</sub> receptor. Dopamine agonists are known to cause somnolence with rates ranging from 20% to 40% in clinical trials. The Epworth Sleepiness Scale (ESS) was more precise than adverse event (AE) reporting and was used to assess somnolence with sumanriole.

**Methods** Somnolence was evaluated in 2 double-blind, randomised, placebo-controlled studies. Both studies had 7-week escalation and 4-week maintenance phases. Early disease patients (Hoehn & Yahr I–III, no levodopa, sumanriole n=78, placebo n=68) were titrated to a fixed dose (0, 2, 8, 24, or 48

mg/day). Advanced disease patients (Hoehn & Yahr II–IV, on levodopa, sumanirole n=125, placebo n=132) were titrated to their optimum dose (1, 2, 4, 8, 16, 24, 32, 48 mg/day, flexible dose study).

**Results** In early disease, the percentage of patients whose ESS scores were  $\geq 15$  (marked drowsiness) at the optimum dose (8 mg/day) were comparable to placebo (0% sumanirole vs 1.5% placebo). The frequency of somnolence reported as an AE was 9.8% at 8 mg/day vs 8.2% in the placebo group. In advanced disease, the percentage of ESS scores  $\geq 15$  were comparable to placebo (4.0% sumanirole vs 4.5% placebo). The frequency of patient-reported somnolence as an AE was 5% vs 1.4% with placebo.

**Conclusions** The incidence of somnolence with sumanirole as measured by the ESS was comparable to placebo. Patient-reported AE rates were much lower than those for other dopamine agonists, suggesting that somnolence is not a major side effect of sumanirole therapy.

#### P 2044

##### **Sumanirole: a highly D2 selective dopamine receptor agonist with efficacy in animal models of Parkinson's disease**

R. B. McCall, N. Nichols, K. Svensson, R. Huff  
*Pharmacia, Kalamazoo, MI, USA*

**Introduction** Dopamine (DA) agonists used to treat Parkinson's disease (PD) bind non-selectively at the D2, D3 and D4 receptors. D3 and D4 receptors may contribute to the psychiatric disturbances which accompany DA agonist and L-DOPA therapeutics. Eliminating D3 and D4 activating properties of DA agonists could reduce the psychiatric and neurological side effects in treating PD.

**Methods** Human D2, D3 or D4 receptors were expressed in CHO cells and utilized in radioligand binding studies and cell based intrinsic efficacy assays. In rats, 6-OH-dopamine (6-OHDA) solution was injected unilaterally into the substantia nigra and tested 2-weeks post lesion. Three cynomolgus monkeys were treated with MPTP IV at different dosages until variable, but stable, Parkinsonian features appeared.

**Results** The affinity of sumanirole for the D2 receptor is  $9.0 \pm 1.0$  nM. Unlike other dopamine agonists, the affinity of sumanirole at D3, D4 and D1 receptors is at least 200-fold lower than at D2 receptors. Sumanirole was a potent full agonist at the D2 receptor but had no activity at D3 and D4 receptors. In 6-OHDA lesioned rats, sumanirole produced a significant dose-related increase in turning. Maximum efficacy of sumanirole was 2.5–5 fold greater than ropinirole, pramipexole, bromocriptine or pergolide. Sumanirole reduced the disability score in MPTP monkeys.

**Conclusions** Sumanirole is the first highly selective D2-receptor agonist developed for the treatment of PD. Clinical studies to date suggest that the enhanced selectivity of sumanirole will result in an improved side effect profile in Parkinson's patients.

#### P 2045

##### **The D2 Pharmacology of Sumanirole**

R. B. McCall, M. Piercey, K. Svensson, V. Sethy  
*Pharmacia, Kalamazoo, MI, USA*

**Introduction** Sumanirole is a highly D2 selective receptor agonist currently under development for the treatment of Parkinson's disease (PD). Unlike other dopamine (DA) ago-

nists, sumanirole binds selectively to the D2 receptor, exhibiting at least 200-fold selectivity for the D2 receptor versus the D1, D3 and D4 receptors. It is hypothesized that enhanced selectivity of sumanirole will reduce the psychiatric and neurological side effects seen with non-selective agonists in treating PD. The objective of this study is to detail the D2 agonist pharmacology of sumanirole.

**Methods** The effects of sumanirole on substantia nigra DA neuron firing were evaluated in anaesthetised rats. Sumanirole's effects on DA metabolism of rat substantia nigra and tuberoinfundibular DA neurons were evaluated. The effects of sumanirole on rat striatal acetylcholine levels were determined. Locomotor and behavioural effects of sumanirole were also studied in rats.

**Results** Sumanirole inhibited the firing of DA neurons in substantia nigra pars compacta with an ED<sub>50</sub> of 0.54 mg/kg, i.v. and decreased DA synthesis and turnover. These effects were blocked by haloperidol. Sumanirole dose-dependently increased striatal acetylcholine levels. Like other DA agonists, sumanirole suppressed exploratory behaviour and induced yawning in the rat at low doses. Sumanirole produced profound locomotor stimulation in habituated and reserpine-pretreated rats compared to other DA agonists and was blocked by haloperidol.

**Conclusions** The D2 agonist properties of sumanirole are supported by the electrophysiological, biochemical and behavioural effects of the drug. Sumanirole differentiated itself from other agonists on the basis of its profound locomotor stimulatory effects.

#### P 2046

##### **Neuroprotective effects of Sumanirole**

R. B. McCall, V. Sethy, H. Wu, J. Oostveen, E. Hall  
*Pharmacia, Kalamazoo, MI, USA*

**Introduction** Sumanirole is a highly D2 selective receptor agonist currently under development for the treatment of Parkinson's disease (PD). PD is characterized by a progressive neurodegeneration of nigrostriatal dopamine neurons, in part caused by oxidative stress. Pramipexole, a dopamine agonist used in PD, has been shown to have neuroprotective properties. Therefore, the objective of the present study was to determine if sumanirole has neuroprotective properties in an animal model of neurotoxicity.

**Methods** 3-acetylpyridine (3-AP), a nicotinamide antagonist, is a potent rat neurotoxin. Sumanirole (1–20 mg/kg, PO) was given either pre- or post 3-AP treatment and animals were sacrificed 96 hours later. Neuronal cell counts were performed in the inferior olive and cGMP, ATP and rotorod performance were used as surrogate toxicity markers.

**Results** 3-AP treatment produced significant decreases in cerebellar cGMP and ATP, decrements in rotorod performance and a significant decrease in inferior olive neurons. Sumanirole, given either before or after 3-AP, significantly attenuated 3-AP induced reductions in cGMP, ATP and rotorod performance in a dose-related manner. Sumanirole also significantly reduced the inferior olive neuronal cell loss produced by 3-AP. Pre-treatment with raclopride did not block the neuroprotective effects of sumanirole.

**Conclusion** Sumanirole has in vivo neuroprotective properties that do not appear to be related to the compound's D2 agonist properties.

P 2047

**Non-compartmental pharmacokinetic (PK) analysis of Sumanitrole in Parkinson's disease (PD) patients**G. A. D'Souza<sup>1</sup>, E. Didier<sup>1</sup>, B. J. Carel<sup>2</sup>, L. J. Schaaf<sup>2</sup><sup>1</sup>Pharmacia Corporation, High Wycombe, UNITED KINGDOM, <sup>2</sup>Pharmacia Corporation, Kalamazoo, MI, USA

**Introduction** Sumanitrole is a potent dopamine D<sub>2</sub> selective receptor agonist in development for treatment of PD. Because of its receptor selectivity, sumanitrole is predicted to have fewer side effects than other dopaminergic agents. A double-blind, placebo-controlled Phase II study was conducted to characterize safety, efficacy and PK of sumanitrole in patients with early PD without levodopa.

**Methods** Following dose titration and a 4-week dose-maintenance period with twice daily extended release oral doses of 2, 8, 24 and 48 mg/day sumanitrole, 6–9 blood samples/patient were collected from 60 patients at extended-stay visits at the end of dose escalation and dose maintenance (Weeks 8 and 11). Sumanitrole plasma concentrations were measured using a validated HPLC method. Data were analysed using Kinetica<sup>®</sup> and non-compartmental analysis (NCA).

**Results** Trough concentrations and maximum concentrations (C<sub>max</sub>) increased dose proportionally across the daily dose range of 2–48 mg. Time to C<sub>max</sub> was variable, ranging from 1–8 h. Mean AUC 1–12 h values of 49, 194, 539 and 1036 ng.h/mL at 2, 8, 24 and 48 mg/day showed dose proportional increases with interindividual variability of 35–64%. No change in PK parameters was seen at weeks 8 and 11, indicating no time-dependent effect. AUC estimates using NCA were very similar (less than 11% difference in means) to estimates made using a population PK approach.

**Conclusion** Sumanitrole pharmacokinetics in early PD patients were dose proportional over a daily dose range of 2–48 mg and no time-dependent changes were observed.

P 2048

**Novelty seeking in patients with Parkinson's disease**O. Novakova<sup>1</sup>, M. Preiss<sup>2</sup>, J. Roth<sup>1</sup>, O. Vesela<sup>1</sup>, E. Ruzicka<sup>1</sup><sup>1</sup>Charles University, Movement Disorders Centre, Prague, CZECH REPUBLIC, <sup>2</sup>Charles University, Prague Psychiatric Centre, Prague, CZECH REPUBLIC

Parkinson's Disease (PD) is thought to be related to certain personality traits. It has been hypothesized that the dopaminergic deficit of patients with PD is associated with a reduction in the dopamine dependent personality dimension novelty seeking (1). The aim of our study was to confirm the concept that novelty seeking is reduced in patients with PD in comparison with other neurological patients and healthy controls. We interviewed 37 patients with PD, 26 patients with essential tremor (ET) and 36 healthy persons. The Cloninger's Temperament and Character Inventory (TCI) was used as method for testing personality dimensions. For statistical analysis, Kruskal-Wallis test was used. Our results did not show difference in novelty seeking between patients with PD and healthy controls. Patients with PD scored even higher in novelty seeking than patients with ET [ $H(df=2)=6.73$ ;  $p<0.05$ ]. We can conclude that our study did not confirm previous findings (1) suggesting relation between dopaminergic deficit of patients with PD and the personality dimension novelty seeking.

**References**

Menza, MA et al.: Parkinson's disease, personality, and dopamine. *J Neuropsychiatry Clin Neurosci* 1990; 2:282–287.  
Study support GAUK 41/00 and MSMT CEZ J13/98 11110001.

P 2049

**Long-term outcomes of thalamic deep brain stimulation for parkinsonian and essential tremor**M. Kronenburger<sup>1</sup>, W. Fogel<sup>2</sup>, M. Krause<sup>3</sup>, V. Tronnier<sup>4</sup><sup>1</sup>Neurology, Klinikum RWTH Aachen, Aachen, GERMANY, <sup>2</sup>Neurology, Deutsche Klinik für Diagnostik, Wiesbaden, GERMANY, <sup>3</sup>Neurology, University of Heidelberg, Heidelberg, GERMANY, <sup>4</sup>Neurosurgery, University of Heidelberg, Heidelberg, GERMANY

Deep Brain Stimulation [DBS] of the thalamic Nucleus ventralis intermedialis [VIM] is a treatment for medically intractable tremor. Little data is available about long-term outcomes.

Over the past 7 years, 18 patients with tremor dominant Parkinson's disease [tPD] and 15 patients with essential Tremor [ET] obtained DBS-implants. 19 Patients were followed over 5 years. Functional disability was evaluated through the score "Activities of Daily Living", from the "Clinical Rating Scale for Tremor". DBS efficacy on tremor was classified "no tremor", "tremor reduction", or "no effect".

Functional disability improved in tPD from 14+/-6 presurgery to 9+/-4 one year postsurgery, to 9+/-6 five years postsurgery; in ET from 19+/-7 presurgery to 8+/-6 one year postsurgery, to 13+/-5 five years postsurgery. One year postsurgery 72% of tPD and 47% of ET had no tremor, 27% of tPD and 52% of ET had tremor reduction. Five years postsurgery 63% of tPD and 20% of ET had no tremor, 18% of tPD and 60% of ET had tremor reduction. DBS had no effect in 18% of tPD and 20% of ET five years postsurgery. Patients with good outcomes had moderate tremor, normal neuroimaging, and <500mg levodopa/day presurgery.

VIM-DBS had good effects over the first year. This declined, especially in ET. It is unclear if other DBS targets lead to better long-term outcomes in ET. tPD patients requiring low doses of levodopa had good outcomes and may be considered for VIM-DBS. Otherwise, DBS of the subthalamic nucleus is recommended as it improves most motor symptoms of PD.

P 2050

**Pergolide can induce spontaneous penile erections and hypersexuality in patients treated for advanced, fluctuating Parkinson's disease**P. Kanovsky<sup>1</sup>, M. Bares<sup>1</sup>, M. Pohanka<sup>2</sup>, I. Rektor<sup>1</sup><sup>1</sup>Masaryk University Brno, St. Anne Hospital, Brno, CZECH REPUBLIC, <sup>2</sup>Teaching Hospital Brno – Bohunice, Brno, CZECH REPUBLIC

Pergolide has been repeatedly shown to be effective and safe treatment in the advanced stage of Parkinson's disease (PD). The complex sexual dysfunction is usually one of the most disabling problems of males suffering from this stage of disease. The effect of dopamine replacement or dopaminergic stimulation on sexual dysfunction in parkinsonian males has already been examined and described in patients treated by L-DOPA or apomorphine, but not by peroral dopamine agonists.

The pergolide mesylate (Permax<sup>®</sup>) was introduced in 32 male patients suffering from advanced, fluctuating PD, who reported also sexual dysfunction. Seven of them (22%) reported important changes of their sexual functions within several weeks of treatment (mean 8, range 6–12) with pergolide.

All these seven patients reported substantial improvement in their motor status, together with relatively sudden onset of hypersexuality. They all were hyperlibidinous, and they were hyperactive in the sexual field asking for sexual intercourse daily. They also reported extraordinarily frequent spontaneous

penile erections, which were present every hour, and lasted almost 30 minutes. The treatment in all patients was manipulated to maintain the motor improvement, and to change the hypersexual behaviour and suppress the spontaneous erections. It seems that pergolide can impressively improve sexual functions in patients with PD. In such cases, the introduction of pergolide might be better choice than the treatment with Sildenafil in younger male patients, who are particularly interested in sexual activities also during the course of Parkinson's disease.

#### P 2051

##### **Clinical impact of diagnostic SPECT investigations with a dopamine reuptake ligand**

A. Lökkegaard, L. M. Werdelin, L. Friberg  
*Bispebjerg Hospital, Copenhagen, DENMARK*

The diagnosis of Parkinson's disease is based on clinical features with pathological verification. However, autopsy has been found to confirm a specialist diagnosis in only about 75% of cases. Especially early in the course of the disease, the clinical diagnosis can be difficult.

Imaging of dopamine presynaptic transporters (DAT receptors) has provided a possible diagnostic probe in the evaluation of Parkinson's disease. The cocaine analogue 123-I-β-CIT is one of several radioligands that have been developed for Single Photon Emission Tomography (SPECT).

The purpose of this study has been to evaluate the impact of 123-I-β-CIT SPECT on the management and diagnosis of patients with parkinsonism.

We have made a retrospective evaluation of the clinical records of 90 consecutive patients referred to 123-I-β-CIT SPECT from the neurological department, Bispebjerg Hospital.

In 58 subjects the scans revealed altered tracer uptake consistent with Parkinson's disease, PSP and MSA. A significant change in the management or treatment because of the scan was found in 25 patients (28%). The sensitivity of the examination was 97% and the specificity 83%.

**Conclusion** A significant clinical impact of DAT receptor imaging was found. DAT receptor imaging is a useful diagnostic probe in patients with a possible diagnosis of parkinsonism.

#### P 2052

##### **Hypothesis: Developmental form of parkinsonian syndrome**

P. Riederer<sup>1</sup>, P. Foley<sup>2</sup>

<sup>1</sup>*Clinical Neurochemistry and NPF Center of Excellence, Department of Psychiatry, University of Würzburg, Würzburg, GERMANY*, <sup>2</sup>*Clinical Neurochemistry, Department of Psychiatry & Institute for the History of Medicine, University of Würzburg, Würzburg, GERMANY*

Despite intensive research, the aetiology of "idiopathic" Parkinson's disease remains unresolved. It has been suggested that certain apparently innocuous viral infections may elicit in the medium to longer-term neurological deficits; conversely, parkinsonism is among the neurological consequences which can follow viral or bacterial encephalitis. It is especially interesting that many viruses associated with encephalitis exhibit a predilection for the extrapyramidal system. Further, the perinatal period is recognized as critical in the normal development

of specific brain regions; exposure to viral infection or other environmental stressors during this period is associated with abnormalities at both the structural and biochemical levels. Specific consequences of such exposure reflect interactions between individual genetic susceptibility, relative vulnerabilities of particular brain regions and the developmental stage at which exposure occurred. Behavioural syndromes reported in children exhibiting early life post-infection neurological damage are generally characterized by relative *hyperactivity*. Children exhibiting reduced motor activity, however, might not attract the same attention, as their behaviour would not be regarded as problematic from a pedagogic point of view; Huffmann (1968) described, for instance, a "defect syndrome" in post-encephalitic children characterized by "*generally friendly, cooperative, attentive individuals, who fitted well into their home environment.*" Further, Widhalm (1985) reported a hypokinetic/parkinsonoid syndrome in children who had experienced overt problems in utero. We propose that such a syndrome in individuals less than twenty years of age may represent a developmental form of parkinsonism attributable to environmental and genetic factors, and that its incidence is underestimated due to greater community concern with overactive children.

#### P 2053

##### **Expression of glutathione-S-transferases in blood of Parkinson's disease patients**

M. Kuzma<sup>1,2</sup>, B. Kazmierczak<sup>3</sup>, E. Usarek<sup>3</sup>, Z. Jamrozik<sup>2</sup>, A. Baranczyk-Kuzma<sup>3</sup>

<sup>1</sup>*Postgraduate School of Molecular Medicine, Warsaw, POLAND*, <sup>2</sup>*Department of Neurology, Medical University of Warsaw, Warsaw, POLAND*, <sup>3</sup>*Chair and Department of Biochemistry, Medical University of Warsaw, Warsaw, POLAND*

Despite extensive research, the aetiology of Parkinson's disease (PD) remains unknown and pathogenesis poorly understood. The key pathologic characteristic of PD is a degeneration of the nigrostriatal tract. Among many factors believed to be responsible for the development of PD, there are the oxidative stress and environmental toxins. Glutathione-S-transferases (GST, EC 2.5.1.18) are the most important detoxification enzymes that inactivate a large variety of compounds including organic peroxides. The **aim** of the present work was to examine the expression of GST isoforms in PD. Studies were conducted on serum and peripheral blood mononuclear cells (PBMC) obtained from blood of PD patients treated with levodopa and dopamine agonists and of healthy blood donors (controls).

**Results** There was no significant difference in serum GST activity between the group of PD patients (n=40) and the age-matched healthy blood donors (n=30). Western blot analysis revealed increased levels of GST mu and alpha in serum of PD patients but decreased level of the main isoform, GST pi, in both serum and PBMC. RT-PCR demonstrated higher expression of GST mu (4 and 5), alpha and pi in PBMC when compared to controls. The results were statistically significant.

**Conclusion** Overexpression of GST mu and alpha may be a physiological response to toxic compounds, including radical oxygen species, formed in Parkinson's disease. The increased expression of GST pi mRNA, not accompanied by the rise of the protein level, may be explained by altered protein translation or increased protein turnover.

P 2054

**Peripheral markers of apoptosis in Parkinson's disease: the effect of dopaminergic drugs.**

F. Blandini<sup>1</sup>, M. Cosentino<sup>2</sup>, A. Mangiagalli<sup>1</sup>, F. Marino<sup>2</sup>, A. Samuele<sup>1</sup>, E. Rasini<sup>2</sup>, R. Fancelli<sup>1,2</sup>, E. Martignoni<sup>3</sup>, G. Riboldazzi<sup>2</sup>, D. Calandrella<sup>2</sup>, G. M. Frigo<sup>4</sup>, G. Nappi<sup>5,1</sup>  
<sup>1</sup>IRCCS "C. Mondino", Pavia, ITALY, <sup>2</sup>University of Insubria, Varese, ITALY, <sup>3</sup>University of Piemonte Orientale "A. Avogadro", Novara, ITALY, <sup>4</sup>University of Pavia, Pavia, ITALY, <sup>5</sup>University "La Sapienza", Rome, ITALY

Apoptosis may play a central role in the neurodegenerative process of Parkinson's disease (PD). Experimental studies have suggested that L-DOPA, still the first choice therapy for the disease, may have pro-apoptotic effects, as a result of its oxidant properties. Conversely, dopamine agonists – which are now currently used for PD treatment, mainly as adjunct therapy – have shown neuroprotective effects. In this study, we investigated pro- and anti-apoptotic proteins in peripheral blood lymphocytes of PD patients under therapy with L-DOPA – alone or in association with dopamine agonists – and age-matched controls. We measured activity of caspase-3 (activator of the apoptotic cascade), levels of anti-apoptotic protein Bcl-2 and expression of the peripheral benzodiazepine receptor (PBR), which is thought to represent the intra-cellular binding site for Bcl-2; we also measured lymphocyte levels of anti-oxidant enzyme superoxide dismutase (Cu/Zn SOD). PD patients showed higher caspase-3 activity and lower levels of Bcl-2, compared to controls. Significant differences were observed between the two groups of PD patients, with patients under treatment with L-DOPA plus dopamine agonists showing lower levels of caspase-3 activity and Bcl-2 than patients taking L-DOPA alone. PD patients showed increased PBR expression, compared to controls, with the patients under treatment with dopamine agonists showing the highest values. In addition, patients treated with L-DOPA alone showed marked increase in Cu/Zn SOD levels. In conclusion, PD patients showed increased expression of peripheral pro-apoptotic markers, compared to healthy subjects. This condition was partially counteracted by the presence of dopamine agonists in the therapeutic regimen.

P 2055

**FP-CIT (DaTSCAN) SPECT in the differential diagnosis of parkinsonism, a study of 25 cases**

J. Vaamonde, R. Ibáñez, A. Soriano  
 Nuestra Señora Alarcos, Ciudad Real, SPAIN

**Introduction** Separating parkinsonian syndromes, using clinical criteria alone, can be difficult. In other way, discrimination of parkinsonian syndromes is important in view of differences in prognosis and therapy, but structural imaging (CT, MRI) is of limited value for differentiating parkinsonian syndromes. We report I-FP-CIT (DaTSCAN) SPECT studies of the presynaptic nigrostriatal dopaminergic neurons, in patients with parkinsonism of different aetiology.

**Patients and method** 25 parkinsonian patients were selected on the basis of bradykinesia, rigidity or tremor.

**Results** A – Tremor was the principal symptom of 10 patients. The study was normal in 6 patients and the diagnosis was essential tremor (ET). 4 patients had abnormal scans and treatment with levodopa was initiated with good response. B – Multiple system atrophy was the clinical diagnosis in 5 cases. DaTSCAN was normal in 3 of them and pathological in 2 cases, these 2 patients improved with levodopa. C – 6 patients showed parkin-

sonism and vascular lesions in the TAC, DaTSCAN was normal in 4 patients (vascular parkinsonism) and pathological in 2 (Parkinson's disease and vascular lesions). D – Depression had been the clinical diagnosis in 4 patients. Abnormal and asymmetrical DaTSCAN SPECT imaging changed the diagnosis to early Parkinson's disease.

**Discussion** I-FJP-CIT SPECT imaging has utility in the diagnosis in patients with parkinsonism and differentiating them from ET. In Multiple System atrophy is not clear whether it is possible to make a distinction in individual cases on the basis of the results of imaging studies of the nigrostriatal pathway alone. DaTSCAN in vascular parkinsonism revealed conflicting results.

P 2056

**DaTSCAN in differential diagnosis of parkinsonian syndromes**

K. Zarubova<sup>1</sup>, E. Ruzicka<sup>2</sup>, J. Roth<sup>2</sup>, K. Kupka<sup>3</sup>, H. Krizova<sup>3</sup>, O. Lang<sup>3</sup>, M. Bojar<sup>1</sup>

<sup>1</sup>Dept. of Neurology, Motol Hospital, Prague, CZECH REPUBLIC, <sup>2</sup>Charles University, Movement Disorders Centre, Prague, CZECH REPUBLIC, <sup>3</sup>Charles University, Dept. of Nuclear Medicine, Prague, CZECH REPUBLIC

Parkinson's disease (PD) is characterised by the loss of dopaminergic neurons in the substantia nigra and decreased dopamine in the striatum. Usually, the diagnosis of PD can be based on the presence of cardinal clinical signs and the response to dopaminergic treatment. In cases presenting with unusual combinations of signs or unclear treatment response, dopamine system can be visualised by DaTSCAN, a SPECT method based on specific binding of FP-CIT, a cocaine analogue labelled by <sup>123</sup>I, to presynaptic dopaminergic transporters. We investigated 21 patients (13 men, 8 women, mean age 53, range 36–79). After intravenous administration of FP-CIT, the distribution of radioactivity in the brain was measured using gamma camera with subsequent visual and semiquantitative evaluation. Based on the results, the patients could be divided into following subgroups:

- 1) Patients without clear response to L-DOPA, showing on DaTSCAN
  - a) unilateral deficit of radioactivity accumulation in the striatum (9 subjects) – confirming the diagnosis of PD;
  - b) bilateral reduction of striatal binding (6 subjects) – reflecting advanced PD or wider involvement of basal ganglia in other neurodegenerative disorders;
  - c) bilaterally normal accumulation of radioactivity (2 subjects) – excluding PD, e.g. in patients with essential tremor;
- 2) Patients with good clinical response to L-DOPA therapy showing bilateral deficit of radioactivity in the striatum (4 subjects), confirming the diagnosis of PD.

In conclusion, DaTSCAN is a functional assessment of presynaptic dopaminergic system improving the diagnostic accuracy of PD, especially in cases with uncertain response to dopaminergic therapy or with atypical clinical features.

P 2057

**Clinical effects of increasing the daily Pergolide dose in pre-treated patients with idiopathic Parkinson's disease (PD)**

H. P. Hundemer, S. Beyenburg, M. Rubin, J. Czekalla, M. Kluge, R. W. Dittmann  
 Lilly Deutschland GmbH, Bad Homburg, GERMANY

**Introduction** Many PD patients are treated with suboptimal doses of pergolide ranging from 0.75 to 1.25 mg/day. The present study evaluates the efficacy and safety of a 0.5 mg pergolide dose increase in PD patients.

**Methods** In this open label multicenter trial patients with a diagnosis of PD were pre-treated with stable doses of levodopa and pergolide (range 0.75–2mg/day). UPDRS Part III motor score was at least 18. The daily pergolide dose was increased by 0.5 mg/day in two 0.25 mg steps over a 4-week period, daily levodopa dose was kept stable. Primary efficacy measure was the change in the UPDRS Part III score from baseline to endpoint after a total of 4 weeks. Other efficacy measures included the UPDRS total score, CGI, and PGI.

**Results** Mean patient age was 64.5 years (females N=33, males N=78). 96 patients completed the protocol. Mean pergolide dose at baseline was 1.21±0.53 mg/day. The UPDRS total score (baseline: 49.4±18.7; endpoint 37.1±19.6, p<0.01) and UPDRS Part III score (baseline: 33.0±12.5; endpoint: 24.2±13.1, p<0.01) significantly improved. Adverse events included dizziness, nausea, sweating, asthenia, and diarrhoea. No serious adverse events were reported.

**Conclusions** Increasing the daily pergolide dose by 0.5 mg in PD patients pre-treated with levodopa and low daily doses of pergolide leads to significant improvements in PD symptoms as measured by the UPDRS total score and UPDRS Part III motor score. The dose increase appeared to be safe and well tolerated.

#### P 2058

##### **Clinical criteria in the treatment of the Parkinson's disease**

B. Schwartz<sup>1</sup>, C. Pantelie<sup>1</sup>, A. Schoenfeld<sup>2</sup>

<sup>1</sup>Clinical Practice, Duisburg, GERMANY, <sup>2</sup>Dept. of Neurology II, University of Magdeburg, Magdeburg, GERMANY

The treatment of Parkinson's disease (PD) with L-dopa has revealed unfavourable effects 5–10 years after the beginning of the therapy. This has led to the present criteria for treatment of *de novo* patients with PD which mainly relay on the age, and aim to delay the use of L-dopa as long as possible. In a retrospective study data of 155 patients with PD were analysed with the goal of finding a clinical marker for the critical time point when the administration of L-dopa turns to be necessary. We presumed that this marker could be the clinical stage of PD. The clinical stage was assessed using the Hoehn & Yahr (H&Y) scale and the severity of the symptoms using the UPDRS. We found no relationship between the age and the kind of the therapy (dopaminagonists vs. L-dopa) with regard to the clinical outcome. However, a significant interaction was found between the clinical stage and the UPDRS score on the one hand and the therapy on the other. In the H&Y stages 1 to 2.5 the UPDRS scores in patients treated only with dopaminagonists was lower than in patients treated with L-dopa while in the H&Y stage and up the UPDRS scores were lower in the patients treated only with L-dopa. The results show that the clinical stage might be a better criterion than the age to appraise the time point when L-dopa needs to be administrated in *de novo* patients with PD.

#### P 2059

##### **Estimation of attentional resources in Parkinson's disease**

S. Hocherman<sup>1</sup>, R. J. Moont<sup>1</sup>, M. Schwartz<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Technion Institute, Haifa, ISRAEL,

<sup>2</sup>Department of Neurology, Bnai Zion Medical Center, Haifa, ISRAEL

Parkinson's disease (PD) involves cognitive changes from its early stages, which involve executive functions, and may include specific attentional impairments. We tested the attentional capabilities of 26 early PD patients and 21 age-matched controls with a new computer based visuo-motor-attention test (VMAT). Testing included a baseline condition of tracking a 1cm circular target that moved along a sinusoidal or a circular path on a computer screen, by moving a cursor, using an unseen manipulum. The baseline condition was followed by several experimental conditions in which various numbers of distractor targets and/or distractor cursors interacted with the real target and cursor. The cost of having to cope with distraction was computed by subtracting performance in the baseline condition from that in the experimental conditions.

Baseline performance of the patients was significantly inferior to controls. A significant decline in performance was found with increasing distraction in both patients and controls. However, distraction had a significantly greater effect on the controls. Still, in the distracted conditions performance of the patients was significantly worse than the controls. In fact, performance of the controls under distraction was still better than the baseline performance of the patients.

These results suggest that PD patients have low attentional resources, which limits their baseline performance and therefore imposes a bottom effect on their performance.

#### P 2060

##### **Rivastigmine is effective and well tolerated in the treatment of Parkinsonian psychosis of geriatric patients**

C. Loos<sup>1</sup>, M. Wening<sup>2</sup>, C. Steinwachs<sup>2</sup>

<sup>1</sup>Klinikum Karlsbad-Langensteinbach, Karlsbad, GERMANY,

<sup>2</sup>Klinikum am Europakanal – Gerontopsychiatrie, Erlangen, GERMANY

**Introduction** Cholinesterase inhibitors are established in the treatment of Alzheimer's disease. The usefulness in dementia with Lewy bodies and in patients with dementia and Parkinson's disease (PD) is also reported. Deterioration of extrapyramidal signs could not be found in those patients, although anticholinergics are effective in controlling motor symptoms in PD.

Elder PD-patients often experience hallucinations, associated with cognitive impairment. Atypical neuroleptics do not ameliorate cognitive functions. Clinical experience suggests that anticholinergics have to be discontinued at first, if psychosis appears. Today, the use of anticholinergics is rare, but it is a new strategy, to add a cholinergic substance such as rivastigmine to the dopaminergic medication in Parkinsonian psychosis.

**Methods** We selected gerontopsychiatric patients, who presented Parkinsonian symptoms and signs of psychosis. These five patients received rivastigmine. Dopaminergic treatment was not changed.

**Results** Patients aged from 75 to 92 had no or mild dementia. Comorbidity did not limit the treatment. Three patients remained on 3, one was up-titrated to 6 and one to 7.5 mg rivastigmine daily during hospitalisation. Psychiatric symptoms disappeared in all cases. All patients tolerated the cholinergic agent well; there were no adverse events which led to reduction or discontinuation of rivastigmine.



**Conclusions** The cholinergic agent rivastigmine reduces neuropsychiatric symptoms when given to elder PD-patients without deteriorating motor function and is well tolerated. This provides a new approach, but does not substitute the need of atypical neuroleptics. More PD-patients should be treated to find out who benefits more from cholinergic than from atypical neuroleptic medication or needs both.

P 2061

**Population pharmacokinetics (PPK) of Sumanitrole in Parkinson's disease (PD) patients**

G. A. D'Souza<sup>1</sup>, J. S. Owen<sup>2</sup>, K. Liolios<sup>2</sup>, B. J. Carel<sup>3</sup>, L. J. Schaaf<sup>3</sup>

<sup>1</sup>Pharmacia Corporation, High Wycombe, UNITED KINGDOM, <sup>2</sup>Cognigen Corporation, Buffalo, NY, USA,

<sup>3</sup>Pharmacia Corporation, Kalamazoo, MI, USA

**Introduction** Sumanitrole is a dopamine D2 selective receptor agonist in development for treatment of PD. Because of receptor selectivity, sumanitrole is predicted to have increased efficacy and fewer side effects than other dopaminergic agents. Two double-blind, placebo-controlled Phase II studies were conducted to characterize the safety, efficacy and PPK of extended release sumanitrole (2–48 mg/day, BID) in patients with early PD or with advanced PD with levodopa.

**Methods** A PPK model was developed using NONMEM® to characterize sumanitrole PPK and the relationship of subject demographics and baseline covariates on PPK variability. Phase I data from healthy volunteers was incorporated for model development.

**Results** PPK data included 378 patients with normal to severely impaired renal function and 20 healthy volunteers. Sumanitrole PPK were described by a one-compartment model with first-order absorption. Volume of distribution ( $V/F$ ) was fixed to a constant 300 L due to correlation with the absorption rate constant. Apparent clearance ( $CL/F$ ) estimates were not sensitive to fixed  $V/F$ .  $CL/F$  was significantly related to creatinine clearance ( $CrCL$  [p<0.001]). A gender effect accounted for a difference of <15% on  $CL/F$ . At a  $CrCL$  of 75.8 mL/min, sumanitrole  $CL/F$  was 23.1 L/hr (males) and 20.1 L/hr (females). With  $CrCL$  and gender in the model, age, race, weight, patient status (healthy volunteer vs PD patient) and levodopa were not significant predictors of  $CL/F$ .

**Conclusions** Sumanitrole disposition in PD patients was primarily influenced by renal function ( $CrCL$ ), only slightly by gender and not by other covariates (age, weight, race, patient status, levodopa therapy).

P 2062

**Evaluation of Sumanitrole pharmacokinetics in non-clinical species, human volunteers and patients with Parkinson's disease: Evidence of linear pharmacokinetics across species**

J. A. Ware<sup>1</sup>, G. A. D'Souza<sup>2</sup>, W. Zhong<sup>1</sup>, M. E. Guyton<sup>1</sup>, L. J. Schaaf<sup>1</sup>, J. N. Duncan<sup>1</sup>

<sup>1</sup>Pharmacia, Kalamazoo, MI, USA, <sup>2</sup>Pharmacia, High Wycombe, UNITED KINGDOM

**Objective** To describe the pharmacokinetics (PK) and disposition of sumanitrole in non-clinical species and human subjects.

**Background** Sumanitrole is a potent D<sub>2</sub> selective agonist at the dopamine receptor ( $K_i=9$  nM) currently in clinical trials for the treatment of Parkinson's disease (PD).

**Design/Methods** Sumanitrole PK and disposition of [<sup>14</sup>C]sumanitrole were evaluated in non-clinical species in separate studies of similar design, and also following administration of an immediate-release (IR) formulation to healthy volunteers and PD patients.

**Results** Sumanitrole was generally well absorbed with an absolute oral bioavailability of >65% in mice, rabbits, and monkeys, and 34% in rats. Absorption-rate limited kinetics were observed after oral dosing in preclinical species. The volume of distribution of sumanitrole was consistent with extensive tissue distribution. Binding to plasma proteins was minimal (<20% across species). Following single and multiple oral dosing, all species displayed dose-proportional increases in plasma concentrations, and exposure to parent compound accounted for 50%–70% of total drug-related radioactivity. The half-life of total radioactivity in human plasma (4.4±0.74 h) was similar to that of parent compound (4.1±0.72 h). Urinary excretion was the primary route of elimination of drug-related radioactivity (79%–92% of dose). PK characteristics in patients with moderate to advanced PD receiving an IR formulation were similar to those in healthy volunteers.

**Conclusions** Sumanitrole is well absorbed, widely distributed, and displays linear PK across non-clinical species and humans. Parent compound was the major drug-related material in plasma following administration to non-clinical species, healthy volunteers, and PD patients.

P 2063

**In vivo and in vitro investigation(s) of Sumanitrole clearance in humans: Sumanitrole exhibits low drug-drug interaction potential**

J. A. Ware, J. P. Sams, M. A. Wynalda, M. P. Grillo, L. C. Wienkers, J. N. Duncan

Pharmacia, Kalamazoo, MI, USA

**Objective** To investigate sumanitrole's mechanisms of clearance and potential for drug-drug interactions (DDI).

**Background** Potency and selectivity of agonists at the D<sub>2</sub> dopamine receptor are important in the development of clinically useful agents for the treatment of Parkinson's disease (PD). In addition, ideal agents should possess desirable ADME characteristics, low potential for DDI, and not be subject to pharmacogenetic differences in drug disposition.

**Methods** The metabolism and disposition of [<sup>14</sup>C]sumanitrole were evaluated in healthy volunteers. In vitro techniques using individual and pooled human liver microsomes, cloned cytochrome P-450s (CYPs), and human hepatocytes were used to investigate the enzymes responsible for sumanitrole metabolism. A comparison of in-vitro and in-vivo metabolite profiles of sumanitrole was also conducted.

**Results** Approximately 50% of sumanitrole was eliminated unchanged in the urine after administration of [<sup>14</sup>C]sumanitrole. Multiple metabolites accounted for the remainder of drug clearance. There was favourable agreement in the rank-order abundance of metabolites formed in vivo with those produced via in vitro systems. In particular, multiple CYPs were involved with sumanitrole metabolism and sumanitrole was not found to be an inhibitor of CYPs. Moreover, all CYP pathways have an apparent  $K_m$  of 300–5000 uM.

**Conclusions** Sumanitrole undergoes multiple metabolic pathways of drug clearance as well as renal excretion. Since PD patients are subject to polypharmacy, the ability to predict DDI using an in vitro approach is helpful. Sumanitrole has a low

potential to inhibit CYPs and is not subject to pharmacogenetic differences of drug metabolising enzymes; ideal properties for a dopaminergic agonist.

#### P 2064

##### **Sumanriole, a new dopamine agonist for the treatment of Parkinson's disease**

C. Wright<sup>1</sup>, B. Gomez-Mancilla<sup>1</sup>, L. J. Schaaf<sup>2</sup>, J. P. Bennett<sup>2</sup>, R. Pahwa<sup>3</sup>, M. F. Lew<sup>4</sup>, W. J. Weiner<sup>5</sup>, R. F. Pfeiffer<sup>6</sup>

<sup>1</sup>Pharmacia Corporation, Kalamazoo, MI, USA, <sup>2</sup>University of Virginia, Charlottesville, VA, USA, <sup>3</sup>University of Kansas Medical Center, Kansas City, KS, USA, <sup>4</sup>University of Southern California, Los Angeles, CA, USA, <sup>5</sup>University of Maryland, Baltimore, MD, USA, <sup>6</sup>University of Tennessee, Memphis, TN, USA

**Introduction** Sumanriole is a unique dopamine agonist that has selectivity for the D<sub>2</sub>-receptor subtype. The pharmacodynamic treatment effect and side effect profile were evaluated in patients with Parkinson's disease (PD).

**Methods** We studied the tolerability, pharmacodynamics, and pharmacokinetics (PK) of different doses of sumanriole (0, 2, 8 and 24 mg/day; immediate-release oral formulation, 4 times daily for 35 days) in 29 moderate to advanced PD patients receiving levodopa.

**Results** In spite of the small number of patients and patient variability, results indicated that for several endpoints, one or more of the sumanriole treatment groups had change from baseline values that were superior to the changes from baseline values for placebo. These included UPDRS II (mean change -4% in the 24-mg/day group), reduction in levodopa dose (by 76% and 53% in the 2-mg/day and 24-mg/day groups, respectively), foot tapping test, and step-seconds test. Sumanriole was rapidly absorbed with mean peak concentrations within 1.5 hours following drug administration. Sumanriole C<sub>max</sub> and AUC<sub>0-5h</sub> values increased dose proportionally and mean half-life ranged from 3.9 to 4.6 hours. No dose-response relationship was evident for the number or types of adverse events that occurred. Sumanriole did not appear to increase the incidence of orthostatic hypotension, nor did it demonstrate any clinically relevant or meaningful cardiac effects or changes in electrocardiogram parameters.

**Conclusions** Sumanriole was well tolerated and had dose proportional PK. The pharmacodynamic test battery showed evidence of a pharmacodynamic treatment effect for several of the endpoints measured, particularly levodopa dose reduction.

#### P 2065

##### **Pergolide pharmacokinetics in patients with Parkinson's disease**

C. Thalamas<sup>1</sup>, I. Rajman<sup>2</sup>, A. Mackie<sup>2</sup>, m. Bareille<sup>1</sup>, C. Soubrouillard<sup>3</sup>, J. Kulisevsky<sup>3</sup>, S. Descombes<sup>1</sup>, C. Brefel-Courbon<sup>1</sup>, N. Fabre<sup>1</sup>, m. Barbanj<sup>4</sup>, O. Blin<sup>3</sup>, O. Rascol<sup>1</sup>

<sup>1</sup>Clinical Investigation Centre, Departments of Neurology and Pharmacology, Toulouse, FRANCE, <sup>2</sup>European Clinical Pharmacology, Eli Lilly and Company, UNITED KINGDOM, <sup>3</sup>CPCET and Department of Pharmacology, Marseille, FRANCE, <sup>4</sup>Department of Pharmacology, Barcelona, SPAIN

**Rationale** Pergolide is widely used in the treatment of Parkinson's disease, but its pharmacokinetics (PK) is not fully known, as the initial bioanalytical assay was not sufficiently sensitive. A more sensitive assay is now available (lower limit of quantification 10 pg/ml). Understanding pergolide PK is important, especially regarding the recent interest in a "continuous

dopamine stimulation" to explain the genesis of L-dopa-induced long-term motor complications (Olanow et al, TiNS 2000).

**Methods** We performed a 2-month open label, randomised, multiple oral dose escalating and descending study (up to 3 mg/d on a t.i.d. regimen) conducted in 14 Parkinson's disease patients (mean age: 62 yrs). Pergolide was analysed using HPLC with mass spectroscopic detection. Non-compartmental PK analysis was used. Parkinson's disease symptoms were assessed using the UPDRS.

**Results** At steady state pergolide was absorbed moderately fast (T<sub>max</sub>=2 to 3 hours post dose) and was eliminated with a terminal half-life of approximately 21 hours (range 6 to 64 hours). C<sub>max</sub> and AUC appeared to increase proportionally with the dose over the range of 0.5 to 3 mg, with large intersubject variability (approximately 50%). Pergolide was well tolerated and no serious adverse events were reported. The mean UPDRS III scores were decreased by up to 8 points while on pergolide.

**Conclusions** The mean pergolide elimination half-life is approximately 21 hours. This finding supports the potential interest for such a drug regarding the hypothesis of central continuous dopamine stimulation in the management of Parkinson's disease.

#### P 2066

##### **The dopamine agonist lisuride provides protection against the deleterious effects of glutamate on dopaminergic neurons**

G. Gille<sup>1</sup>, G. Xu<sup>1</sup>, A. Uhlig<sup>1</sup>, W. Rausch<sup>2</sup>, B. Janetzky<sup>1</sup>, A. Engler<sup>3</sup>, H. Reichmann<sup>1</sup>

<sup>1</sup>Technical University Dresden, Dresden, GERMANY, <sup>2</sup>Veterinary Medical University, Vienna, AUSTRIA, <sup>3</sup>Schering Deutschland GmbH, Berlin, GERMANY

**Introduction** Glutamate excitotoxicity is discussed as a contributing factor to Parkinson's disease. We recently showed the protective effects of the high affinity D<sub>2</sub> receptor agonist lisuride on dopaminergic neurons. We investigated if lisuride was also able to protect against glutamate toxicity.

**Methods** Dopaminergic neurons in primary culture were pre-treated with lisuride (0.001–10 microM) on the 8th day in vitro (DIV) for 24 h. On the 9th DIV glutamate (0.5 mM) was added for 10 min and the survival rate of dopaminergic neurons was determined following a 2-day period of recovery. Alternatively, lisuride was added directly after glutamate treatment during the 2 days of recovery. The D<sub>2</sub> antagonist sulpiride was co-administered with lisuride on the 8th DIV. Antioxidative properties of lisuride were tested by preventing the autoxidation of 200 microM L-DOPA.

**Results** Glutamate reduced the number of dopaminergic neurons by 69%, while lisuride reduced cell loss by 51% at 0.1 microM when added 24 h before glutamate. Simultaneous addition of sulpiride prevented the effect of lisuride. Even when added after glutamate treatment, lisuride reduced cell loss by 54% at 0.1 microM.

Lisuride suppressed autoxidation of L-DOPA by 80% at 1 mM being even more potent than vitamin C (53% reduction).

**Conclusion** These data imply that lisuride exerts neuroprotective effects on dopaminergic neurons in primary culture against glutamate excitotoxicity. Stimulation of the D<sub>2</sub> receptor seems to play a role, since sulpiride abolished the protective effects. The inhibitory effect of lisuride on L-DOPA autoxidation indicates direct antioxidative properties of the agonist.

P 2067

**Ginsenosides Rb1 and Rg1 effects on neurite growth and survival of glutamate affected dopaminergic cells**K. Radad<sup>1</sup>, G. Gille<sup>2</sup>, C. Luo<sup>3</sup>, H. Saito<sup>4</sup>, W. D. Rausch<sup>1</sup><sup>1</sup>Med.Chem.Vet.Med. University, Vienna, AUSTRIA,<sup>2</sup>Department of Neurology, Technical University, Dresden, GERMANY, <sup>3</sup>Jilin University, Jilin, CHINA, <sup>4</sup>Coll. Pharm., Nihon University, Chiba, JAPAN

Ginsenosides Rb1 and Rg1 as an important and active principle of ginseng extract (*Panax ginseng* C.A. Meyer, Araliaceae) appear to exert protection against ischaemic and anoxic damage, suggesting an antioxidative and cytoprotective role. This present study was carried out to test the beneficial actions of these two ginsenosides on the survival and neurite outgrowth of dopaminergic cells affected with the excitotoxicant glutamate. Dopaminergic cultures were prepared from embryonic mouse mesencephala cultured first in DMEM (Dulbecco's Modified Eagle's Medium) containing 10% fetal calf serum and switched at DIV (day in vitro) 6 to serum free condition. Cultures were grown at 37°C with an atmosphere of 5% CO<sub>2</sub> for 11 days. Cultured cells were treated according to the following protocols: i) untreated control. ii) glutamate group: cells were exposed to 0.5 mM glutamate for 15 minutes at day 9. iii) ginsenoside groups: 10 mM of either ginsenosides were added to the medium from day 6 and with glutamate at day 9. Exposure of cultures to excess glutamate (0.5 mM) caused extensive death of dopaminergic cells by 68–76% compared to control. Ginsenoside Rb1 (not Rg1) significantly enhanced the cell number of mesencephalic dopaminergic cells by 18.09% compared to control. Both ginsenosides Rb1 and Rg1 increased the length of neurites by 10–13% compared to cells exposed to glutamate. Thus, we conclude that ginsenosides Rb1 and Rg1 have a potential for neurotrophic and neuroprotective effects on mesencephalic dopaminergic cells.

P 2068

**Autonomic dysfunction in early stages of Parkinson's disease (P.D.)**P. Vrentas<sup>1</sup>, V. Panayiotopoulou<sup>1</sup>, S. Sameli<sup>1</sup>, V. Kiriakakis<sup>2</sup>, C. Sarantopoulos<sup>1</sup>, A. Andelli<sup>1</sup>, C. Ppadopoulos<sup>1</sup><sup>1</sup>Tripolis Psychiatric Hospital, Tripolis, GREECE, <sup>2</sup>Lamia General Hospital, Lamia, GREECE

**Introduction** Although early severe autonomic involvement should alert the clinician for diagnosis other than P.D., autonomic dysfunction does occur most commonly in late stages. The purpose of this study is to investigate the prevalence of autonomic disturbances in early stages of P.D.

**Methods** Thirty seven patients (19M and 18F) mean age 60 years clinically diagnosed with P.D., Hoehn-Yahr scale score <2 and mean disease duration 3.6 years were studied for autonomic dysfunction in the early stages of their disease. Exclusion criteria were those that Parkinson's Disease Society Brain Bank guidelines include among the elements necessary to reach correct diagnosis.

**Results** A significant percentage of patients studied, 70% (26 patients) complained with at least one Auto-nomic nervous system symptom. Among them, 50% (13 patients) complained for seborrhoea, 77% (20 patients) for Gastrointestinal (G.I.) dysfunction, 42% (8 patients) for Erectile dysfunction, 30.7% (8 patients) for Urinary urgency (but not frank incontinence) and 7.7% (2 patients) for Orthostatic Hypotension (O.H.). Furthermore, among patients who reported G.I. dysfunction, 50% (13 patients) had constipation, 23% (6 patients)

swallowing difficulties but not severe dysphagia and 23% (6 patients) increased salivation. However, elderly patients are expected to develop relatively earlier genitourinary dysfunction than do younger onset patients due to concurrent urological problems.

**Conclusion** Autonomic involvement is a relatively late feature of P.D. However, some "autonomic" problems such as constipation, seborrhoea, erectile difficulties and less frequently impaired swallowing and salivation seem to be present at the early stages of the disease where others (i.e. O.H., severe dysphagia and incontinence) are uncommon.

P 2069

**Parkinsonian syndrome in drug addicts after using intravenous Mn-containing mixture**S. Haldre<sup>1</sup>, S. Lüüs<sup>1</sup>, T. Toomsoo<sup>2</sup><sup>1</sup>University of Tartu, Tartu, ESTONIA, <sup>2</sup>Magdaleena Hospital, Tallinn, ESTONIA

**Introduction** Parkinsonian syndrome can be triggered by drugs, or less frequently by other exogenous substances.

**Methods** The authors report on 4 patients, who were evaluated at the Department of Neurology and Neurosurgery, University of Tartu from 1998 to 2001 due to a rapid development of parkinsonian syndrome. For mood elevating purposes all of them had been intravenously injecting a solution made from pseudoephedrin (Sudafed), acetic acid, KMnO<sub>4</sub> and water.

**Results** The group of patients consisted of two males and two females whose mean age was 21.5 years (19–28). The period over which injections were made before the appearance of the symptoms varied from several months to one year. All the patients developed bradykinesia, hypomimia, impairment of gait and posture. The most severely affected patient was only able to walk using a support. There were rigidity and dystonic movements in her legs with no obvious paresis.

Laboratory data revealed no evident abnormality, except low Cu and ceruloplasmin levels in the worst case. One patient was HIV positive. MRT, EEG showed no marked pathology.

No treatment proved to be effective, no patient showed improved in his or her condition.

**Conclusion** Several reports have described extrapyramidal syndrome in laboratory animals with manganese poisoning. Also, cases of welding-related parkinsonism or parkinsonism due to environmental pollution have been described in literature.

The authors speculate that intravenous administration of highly concentrated manganese solution is the major cause for extrapyramidal syndrome in the reported patients.

P 2070

**Effect of cannabis on Parkinson's disease symptoms: questionnaire-based study**K. Venderova<sup>1</sup>, E. Ruzicka<sup>2</sup>, P. Visnovsky<sup>1</sup><sup>1</sup>Faculty of Pharmacy, Charles University, Hradec Kralove, CZECH REPUBLIC, <sup>2</sup>1st Medical Faculty, Charles University, Prague, CZECH REPUBLIC

Following the information presented in the media we realised some of our patients use cannabis to alleviate their Parkinson's disease (PD) symptoms. To evaluate their possible experience, all patients with PD registered at the Movement Disorder Centre (MDC) were asked to anonymously complete a questionnaire. Out of 630 questionnaires sent, 339 (53.8%) were returned. The responders' mean age was 65.7 years (range; 36–92 years) and the average PD duration 8.6 years (range; <1–46). 85 patients (25.1%) reported to have an experience with cannabis, mostly

using fresh or dried cannabis leaves orally. In this group, 39 patients (45.9%) described mild or substantial alleviation of their PD symptoms in general, 26 (30.6%) improvement of rest tremor, 38 (44.7%) alleviation of bradykinesia, 32 (37.6%) alleviation of muscle rigidity and 12 (14.1%) improvement of levodopa-induced dyskinesias. According to the information obtained from the patients, this alleviation in average occurred 1.7 months (range; 1 hour–6 months) after their first cannabis use. There was a correlation between the duration of cannabis use and feeling of improvement in general PD symptoms ( $p < 0.001$ ,  $\chi^2$  test), rest tremor ( $p < 0.01$ ), bradykinesia ( $p < 0.01$ ) and muscle rigidity ( $p < 0.01$ ). In case of dyskinesias, the beneficial effect did not correlate with the length of cannabis use, but the patients using cannabis with higher frequency reported alleviation of dyskinesias more often ( $p < 0.05$ ). It seems some of the cannabinoids or compounds targeting the cannabinergic system might be useful in the treatment of PD symptoms or drug-induced dyskinesias.

Supported by FRVS grant 2223/02.

#### P 2071

##### Symptom focused questionnaire in Parkinson's disease

G. Medley, M. J. Steiger

*The Walton Centre for Neurology & Neurosurgery, Liverpool, UNITED KINGDOM*

How can we improve the management of Parkinson's disease of patients attending clinic?

The study aimed at improving the quality of care of the Parkinson's disease patient by using a symptom focused questionnaire (SFQ). The questionnaire developed is a modified form of the Unified Parkinson's Disease Rating Scale.

Fifty consecutive patients with Parkinson's disease were sent a questionnaire (SFQ) prior to their outpatient appointment. Patients attended a Movement Disorder Clinic run by a Consultant Neurologist and a Neurology Nurse Clinician. During the consultation the SFQ was then used to augment the consultation process. Following the consultation all patients completed a "General Satisfaction" questionnaire together with a "SFQ Satisfaction" questionnaire.

A comparison group of fifty patients with Parkinson's disease were not sent the SFQ. An assessment of the quality of their appointment was made by completing the General Satisfaction questionnaire only.

Although a minority reported an unnecessary number of enquiries being made during the appointment, all patients reported satisfaction with the consultation. A third of Parkinson's disease patients stated that the SFQ permitted time to reflect upon their symptoms of Parkinson's disease and the totality of symptoms. Thus effectively identifying main causes of concern. The Symptom Focused Questionnaire offers a useful clinical tool in enhancing the outpatient consultation. Patients report that time spent reflecting upon their symptoms, prior to their clinic appointment, effectively assists in identifying their individual needs.

#### P 2072

##### Mental disorders in Parkinson's disease: treatment with quetiapine

C. Pacchetti, F. Mancini, S. Cristina, R. Zangaglia, E. Martignoni, G. Nappi

*Istituto neurologico "C. Mondino", Pavia, ITALY*

Mental Disorders (MDs) are disabling complications of Parkinson's disease (PD). We set out to demonstrate the efficacy

of quetiapine, in controlling MDs without worsening the parkinsonism, and to ascertain whether quetiapine can facilitate the pharmacological management of advanced stages of PD when MDs appear. The effect of quetiapine on specific psychiatric features was also investigated.

Thirty-five PD patients with disabling MDs were enrolled in this open-label study. Evaluation of motor function, of MDs and of cognitive state were completed before starting quetiapine and after 3 months of stable treatment. Dopaminergic drug variations were monitored throughout the study. MDs significantly improved after 3 months of quetiapine treatment at a mean daily dose of 140 mg, without producing significant changes in motor or cognitive function. Our population displayed three distinct MDs: hallucinations alone, which responded best to quetiapine; delirium, which responded to higher doses of quetiapine, and confusional state which showed only a slight response to the drug. Quetiapine was effective for the treatment of MDs in PD, particularly hallucinations and delirium. Quetiapine did not worsen motor functions and allowed the dopaminergic regimen in PD patients affected by MDs to be managed safely.

#### P 2073

##### The analysis of parkinsonian tremor using double axis accelerometer

A. Machowska-Majchrzak<sup>1</sup>, K. Pierzchala<sup>1</sup>, S. Pietraszek<sup>2</sup>

<sup>1</sup>Silesian Medical Academy, Zabrze, POLAND, <sup>2</sup>Silesian University of Technology, Gliwice, POLAND

**Introduction** Tremor is a common symptom of many neurological disorders, including also Parkinson's disease. Objective assessment of tremor indicators – amplitude, frequency, "harmonicity" – is a useful method, which allows discriminating different types of tremor.

**Objective** The aim of the study was development the method supporting the diagnosis in patients with Parkinson Disease (PD) by application spectral analysis of tremor recorded from palm, using accelerometer sensor.

**Material** 17 subjects (11 men and 6 women, age 42–81 years, mean 61.1) with clinically confirmed PD and 10 control subjects participated.

**Method** Recordings were performed with the use of double axis accelerometer and computer interface. Sensor was mounted at the dorsal of palm or fingers. Spectral analysis was done in Matlab of line. Analysis focused on determination shape of spectrum, the frequency of peak, central frequency, and harmonic index (HI).

**Results** In all subjects with clinically confirmed PD the characteristic sharp peak in spectrum was present at frequencies 5.1 to 7.8 Hz. In subsequent epochs the shape of spectrum significantly differs and HI varies from 0.8 to 0.95. In control group the spectrum was wide and consists of many peaks at frequencies from 3 to 8 Hz. The HI was 0.6 to 0.8.

**Conclusion** At the present state of our investigation the spectral analysis of acceleration signal recorded from palm seemed to be promising tool for supporting the diagnosis of Parkinsonian tremor.

#### P 2074

##### Swallowing disorders in Parkinson's disease

A. Potulska-Swidrowska, A. Friedman

*Medical University of Warsaw, Warszawa, POLAND*

**Introduction** Impairment of swallowing is a common symptom in advanced stages of Parkinson's disease, which may cause serious complications. The aim of the study was to compare

oral, pharyngeal and oesophageal phase of swallowing of PD patients with healthy controls.

**Material and methods** Swallowing in 11 PD patients and 9 controls was studied by EMG and oesophageal scintigraphy. 8 patients were aware of swallowing difficulties, while 3 did not complain of any.

**Results** PD patients had delayed triggering of swallowing reflex ( $543 \pm 84$  ms vs.  $230 \pm 66$  ms in controls,  $p < 0.05$ ), longer time of laryngeal movement ( $1880 \pm 140$  ms vs.  $1349 \pm 154$  ms,  $p < 0.05$ ), longer oesophageal phase of swallowing ( $12.4 \pm 2.4$  s vs.  $6.4 \pm 1.2$ ,  $p < 0.001$ ), and much smaller dysphagia limit (the maximum amount of water, which could be swallowed at once – in normal subjects it is  $> 20$  ml) –  $4.5 \pm 0.9$  ml. Dysphagia, as assessed by these methods, was present in all cases studied, even in those who did not complained of swallowing problems.

#### P 2075

##### **Urodynamic abnormalities in patients with Parkinson disease**

I. Martinic Popovic, A. Popovic, Z. Trkanjec, V. Demarin  
*Department of Neurology "Sestre milosrdnice" University Hospital, Zagreb, CROATIA*

**Introduction** Patients with Parkinson disease (PD) often experience voiding dysfunction. In male patients it could be caused by PD itself or by bladder outlet obstruction, while in female patients causes may be complex and not congruent with symptoms.

**Subjects and methods** In our pilot-study urodynamic testing was performed in 15 patients with PD (9 males, 6 females) and International Prostate Symptom (IPS) score. This score reflects voiding dysfunction, not only prostatic symptoms, thus it can be used in male and female patients. Data on disease severity was obtained using UPDRS and Hoehn and Yahr Scale. Disease duration, age, sex and treatment with antiparkinsonian drugs were also recorded.

**Results** Urodynamic testing showed detrusor hyperreflexia in 10 patients, hyporeflexia or areflexia in 2, hyperreflexia with impaired contractile function in 2 and hyperreflexia with detrusor-sphincter dysynergia in 1 patient. Severity of voiding disturbances increased with disease severity, with post-void residual urine volume as the parameter showing the best correlation. IPS scores increased with disease severity. Irritative index score correlated with maximum cystometric capacity and obstructive symptom score with post-void residual urine volume. We found no significant differences regarding age, but obstructive symptoms were prevalent in male patients. Influence of antiparkinsonian drugs was not certain.

**Conclusions** Voiding dysfunction in patients with Parkinson disease progressively worsens with advancing of disability (Hoehn and Yahr Scale  $> 3$ ). Dysfunction of the striated urethral sphincter and pelvic musculature is often seen in PD, and delayed relaxation at the time of initiation of voluntary voiding is the main symptom.

#### P 2076

##### **Excessive daytime somnolence: a follow-up study in de novo Parkinson's disease**

G. Fabbri, P. Barbanti, C. Aurilia, L. Pratesi, P. L. Zuchegna, G. Meco  
*University La Sapienza, Rome, ITALY*

**Introduction** Pathophysiology of excessive daytime somnolence (EDS) in Parkinson's disease (PD) is still debated. Factors related to the disease or to the treatment may be both equally

important. We have previously shown that "de novo" PD patients are not different from healthy sex and age matched controls in measures of EDS. We therefore followed up these patients after the introduction of antiparkinsonian drugs.

**Methods and patients** EDS was assessed by means of the Epworth Sleepiness Scale (ESS) in 25 PD patients (mean age 64.7 years, mean symptoms duration 2.6 years) either at baseline, when untreated, and after 1 year of treatment with different antiparkinsonian medications. Motor disability was measured by means of subset III of the UPDRS scale.

**Results** After 1 year of treatment with antiparkinsonian drugs ESS score significantly increased ( $p = 0.01$ ) from baseline, while motor disability remained stable or improved in most patients as a result of treatment.

**Conclusion** The increase in ESS score and consequently of EDS in this group of patients seems to be related mainly to a direct effect of the treatment.

#### P 2077

##### **Dopamine and depression in patients with Parkinson's disease (PD)**

P. Malitas  
*Eginitio Hospital, Psychiatric Clinic of the Athens University, Athens, GREECE*

**Introduction**  $\approx 40$ – $60\%$  patients with PD experience a Major Depressive Episode (DE) requiring treatment. The pathogenesis may be reduced dopaminergic activity, inadequate serotonin secretion, or psychological reactions. It has been observed that depression in PD patients is related to "off" periods of response to levodopa. Since the dopaminergic system has a role in the formation of emotional state, and low levels of dopamine metabolites (HVA) are found in depressive patients, dopamine may participate in the pathogenesis of affective disorder and that there is a potential role for dopamine agonists (DAs) in depression.

**Methods** Thirty-eight patients with PD were diagnosed with Depressive Disorder (DD) (DSM-IV) with DE. Twenty-two had a history of DD. All patients had received inadequate combination treatment for depression (daily doses of nortriptyline and fluoxetine (40 mg)) for 7 weeks while receiving levodopa for PD in 4 daily doses. Pramipexole (PPX) was added the treatment regime of these patients.

**Results** During the first 3 weeks, HAM-D scores (17 items) were reduced by 18%; at 6 weeks, 48%; at 18 weeks, 53%; at 24 weeks, mean reduction of total score reached 61% in 34 patients (N=38). Two of the patients dropped out due to adverse events.

**Discussion** The antidepressive effect of PPX was evident after the first month of treatment, with a distinct improvement in psychomotor state. Further studies are needed to clarify the role of PPX and the dopaminergic system in the pathogenesis of DD and to determine the patient group that responds to treatment with DAs.

#### P 2078

##### **Excessive daytime sleepiness and "sleep attacks" induced by entacapone- three case reports**

M. Bares, P. Kanovsky, I. Rektor  
*1st Department of Neurology, St. Anne's Hospital, Brno, CZECH REPUBLIC*

**Introduction** "Sleep attacks" are events of overwhelming sleepiness that occur without warning, or that occur with a prodrome that is so short or so overpowering that it prevents the

patient from taking appropriate protective measures. New observations imply that inappropriate daytime sleep episodes are not exclusive to dopamine agonists.

**Methods, patients** Three Parkinson's disease patients reported excessive daytime sleepiness with sudden sleep attacks while receiving entacapone.

**Discussion** In our patients Nos. 1 and 3, there is a strong indication, regarding the time and the diminishment of the sleep attacks after the discontinuation of the entacapone administration that the cause of the induced daytime sleepiness might be the increased bioavailability of L-DOPA, induced by entacapone. This theory is compromised by previous treatment with tolcapone (patient No.2) without any sleep problems. A possible explanation for the differing action of COMT inhibitors could be explained in terms of central affinity or in terms of different pharmacokinetics. The clinical observation of delayed sleep attacks latency after the entacapone introduction, and about of two weeks of waning after entacapone suspension could be the argument for another explanation. Whether this could mean that the sleep attacks might be induced by entacapone itself remain unknown.

**Conclusion** Our conclusion does not exclude the possible role of PD itself rather than merely the medications in this problem. In any case, our experience strongly suggests that the occurrence of sleep attacks is not exclusively limited to patients treated by dopamine agonists.

This research was supported by Research Plan MŠCR 112801.

#### P 2079

##### Is depression a cofactor for dependence and disability in Parkinson's disease?

M. Raisakis-Forstner<sup>1</sup>, K. Petrovic<sup>2</sup>, K. Suppan<sup>1</sup>, Z. Raissakis<sup>1</sup>, K. Wenzel<sup>2</sup>, K. Kern<sup>1</sup>, G. Ivanic<sup>2</sup>, B. Homann<sup>1</sup>, C. Pock<sup>1</sup>, C.N. Homann<sup>1</sup>

<sup>1</sup>Klinik Maria Theresia, Hospital for Neurological Rehabilitation, Bad Radkersburg, AUSTRIA, <sup>2</sup>Dept. of Neurology, University Hospital Graz, AUSTRIA

Twenty percent of patients with Parkinson's disease (PD) suffer from depression (DP). Several symptoms of PD like bradykinesia and lack of facial expression mimic depressiveness so that DP in these patients is often overlooked and under-treated. However it can be assumed that it diminishes further the already reduced quality of life (QoL) and that it leads to a greater degree of disability and dependence, but the magnitude of this effect is not well studied. 164 patients, 77 male and 87 female, aged 69.8±11.5 with PD were investigated with the help of a semi-structured interview with the aim to compare the degree of dependence upon orthopaedic devices, caregivers and social institutions in PD patients with and without depression. The 27.5% of patients that were found to be depressed (Center of epidemiological studies depression scale >23) showed more cognitive impairment (Matis Dementia Rating scale: 33.9 vs. 129.5, p<0.05) but similar age and gender distribution when compared to non-depressed PD patients. The degree of dependence however was not found to be differing significantly between the groups suggesting that the impact of DP on social status and disability might be smaller than anticipated.

## Multiple sclerosis 1

#### P 2080

##### MHC class II transactivator (CIITA)-driven class II expression by astrocytes promotes autopathogenic peptide presentation but not susceptibility to CNS autoimmune disease

O. Stuve<sup>1</sup>, S. Youssef<sup>2</sup>, A. J. Slavin<sup>3</sup>, C. L. King<sup>1</sup>, J. C. Patarroyo<sup>1</sup>, D. L. Hirschberg<sup>2</sup>, J. W. Brickey<sup>4</sup>, J. F. Piskurich<sup>5</sup>, H. A. Chapman<sup>6</sup>, S. S. Zamvil<sup>1</sup>

<sup>1</sup>Department of Neurology, University of California, San Francisco, San Francisco, CA, USA, <sup>2</sup>Department of Neurology, Stanford University, Stanford, CA, USA, <sup>3</sup>Tularik Inc., South San Francisco, CA, USA, <sup>4</sup>University of North Carolina, Chapel Hill, NC, USA, <sup>5</sup>Mercer University School of Medicine, Macon, GA, USA, <sup>6</sup>Pulmonary Medicine, University of California, San Francisco, San Francisco, CA, USA

**Introduction** We examined the role of the MHC class II transactivator (CIITA) in central nervous system (CNS) class II expression and antigen (Ag) presentation by astrocytes and in experimental autoimmune encephalomyelitis (EAE) susceptibility.

**Methods** CIITA-transfected astrocytes, newly generated transgenic (Tg) mice that utilized the glial fibrillary acidic protein (GFAP) promoter to target astrocyte expression of (CIITA), and CIITA-deficient mice were utilized for this study.

**Results** CIITA-transfected astrocytes upregulated class II molecules, whereas IFN $\gamma$ -activated CIITA-deficient astrocytes did not. CIITA-deficient mice were resistant to EAE by immunization with CNS autoantigen. CIITA-deficient APC were capable of presenting peptide to wild-type CD4<sup>+</sup> T cells, indicating the presence of CIITA-independent mechanisms for peripheral T cell priming. Adoptive transfer of wild-type CNS autoantigen-specific CD4<sup>+</sup> T cells into CIITA-deficient mice did not induce EAE, indicating that CIITA-dependent class II expression was required for CNS antigen presentation. GFAP-CIITA-Tg mice did not develop spontaneous EAE, or more severe EAE than control mice when immunized with encephalitogenic peptide. Whereas IFN $\gamma$ -activated astrocytes could present peptide or native antigen, CIITA-transfected astrocytes could present peptide only, indicating that CIITA-transfected astrocytes could not process native antigen. IFN $\gamma$ -activated astrocytes also upregulated cathepsin (Cat) S, whereas unstimulated, CIITA-transfected astrocytes did not.

**Conclusion** Our results demonstrate that although CIITA-directed class II expression is required for CNS Ag presentation and EAE induction, CIITA-directed class II expression alone in astrocytes is not sufficient for Ag processing and does not support induction of CNS autoimmune disease.

#### P 2080a

##### Two genome-wide linkage disequilibrium screens in Scandinavian multiple sclerosis patients reveal association to chromosome regions 1p34, 6p21, 11q23, 12q23 and 19q13

H. Flinstad Harbo<sup>\*1</sup>, P. Datta<sup>\*2</sup>, A. Oturai<sup>2</sup>, L. P. Ryder<sup>3</sup>, S. Sawcer<sup>3</sup>, E. Setakis<sup>4</sup>, D. Clayton<sup>4</sup>, E. Åkesson<sup>5</sup>, E. G. Celius<sup>6</sup>, H. Modin<sup>5</sup>, M. Sandberg-Wollheim<sup>7</sup>, K. M. Myhr<sup>8</sup>, O. Andersen<sup>9</sup>, J. Hillert<sup>3</sup>, P. Soelberg Sørensen<sup>2</sup>, A. Svejgaard<sup>2</sup>, A. Compston<sup>3</sup>, F. Vartdal<sup>1</sup>, A. Spurkland<sup>1</sup>

\*These authors contributed equally

<sup>1</sup>Rikshospitalet University Hospital, Oslo, NORWAY, <sup>2</sup>Copenhagen University Hospital, Rigshospitalet, Copenhagen, DENMARK, <sup>3</sup>University of Cambridge Neurology Unit, Addenbrooke's Hospital, Cambridge, UK, <sup>4</sup>Institute of Public Health, University Forvie Site, Cambridge, UK, <sup>5</sup>Huddinge University Hospital, Huddinge, SWEDEN, <sup>6</sup>Ullevål University Hospital, Oslo, NORWAY, <sup>7</sup>Lund University Hospital, Lund, SWEDEN, <sup>8</sup>Haukeland Hospital, Bergen, NORWAY, <sup>9</sup>Gothenburg University Hospital, Gothenburg, SWEDEN

**Aims and methods** In order to identify genomic regions containing susceptibility genes for multiple sclerosis (MS) we performed the first two genome-wide screens for linkage disequilibrium in the genetically homogenous Scandinavian population, using pooled DNA and a dense map of 6000 microsatellite markers provided through the GAMES (Genetic Analysis of Multiple sclerosis in EuropeanS) collaboration. In the first screen, 199 cases were compared with 200 controls; in the second, a further 201 cases were compared with a second set of 200 controls. In each screen, allele image profiles (AIPs) generated from cases and controls were compared statistically in order to identify those markers showing the greatest evidence for association.

**Results** Data were achieved from 4041 markers in the first screen and from 4228 markers in the second screen. Results for both screens were available in the same 3360 markers. Twenty-three markers showed statistically significant differences between case-control AIPs in both screens. When additional AIPs were generated for these 23 markers, statistical significance was retained for five gene regions, at 1p34 (*MYCL1*), 6p21 (*D6S2447*), 11q23 (*D11S1986*), 12q23 (*D12S377*) and 19q13 (*D19S552*).

**Conclusion** These genome-wide screens for linkage disequilibrium in Scandinavian MS patients identified novel disease associations with four gene regions, at 1p34 (*MYCL1*), 11q23 (*D11S1986*), 12q23 (*D12S377*) and 19q13 (*D19S552*), in addition to confirming the well known association to the HLA class II region (*D6S2447* at 6p21). Several promising MS susceptibility candidate genes are located within these gene regions.

#### P 2081

##### **Surrogate markers for disability in multiple sclerosis: the relation of brain-specific proteins to spinal cord degeneration in chronic relapsing experimental allergic encephalomyelitis**

A. Petzold, D. Baker, G. Pryce, G. Keir, E. J. Thompson, G. Giovannoni  
*Institute of Neurology, London, UNITED KINGDOM*

**Background** Chronic relapsing experimental allergic encephalomyelitis (CREAE) results in spinal cord atrophy. Measurement of brain-specific proteins such as the axonal neurofilaments (Nf), the astrocytic glial fibrillary acidic protein (GFAP)/S100B, and microglial ferritin might allow for quantification of the degenerative process.

**Methods** CREAE was induced in adult Biozzi AB/H mice (6–8 weeks old) and animals were sacrificed 60–80 days post disease induction (CREAE n=9, control n=6). The spinal cords were homogenised and analysed for Nf, GFAP, S100B, ferritin and total protein using in-house assays. Statistical analysis was performed using Spearman's correlation coefficient and Fischer's exact test.

**Results** There was marked gliosis and axonal loss in the spinal cord of CREAE animals. The levels of GFAP were 3-fold increased in CREAE (median: 12.5 ug/mg protein, range: 5.0–26.4 ug/mg protein) when compared to controls (4.0 ug/mg protein, 1.4–4.5 ug/mg protein, p<0.001). The levels of Nf were about 2-fold decreased in CREAE (27 ug/mg protein, 9–84 ug/mg protein) when compared to controls (61 ug/mg protein, 53–79 ug/mg protein, p<0.05). No statistical significant difference was found for levels of S100B and ferritin. However there was a correlation between S100B and Nf (R=0.88, p<0.01) and between ferritin and Nf (R=0.99, p<0.001). No such correlation was found with GFAP.

**Conclusion** Levels of spinal cord neurofilament and GFAP are surrogate markers for axonal degeneration and gliosis, respectively. Because these pathological processes result in clinical disability, these proteins have the potential to be used as secondary outcome measures in neuroprotective treatment studies.

#### P 2082

##### **Multiple sclerosis: immunological effects of mitoxantrone in vitro reveal antigen-presenting cells as major targets**

O. Neuhaus<sup>1</sup>, H. Wiendl<sup>2</sup>, B. C. Kieseier<sup>3</sup>, S. Strasser-Fuchs<sup>1</sup>, F. Fazekas<sup>1</sup>, J. J. Archelos<sup>1</sup>, H. P. Hartung<sup>3</sup>  
<sup>1</sup>Department of Neurology, University of Graz, Graz, AUSTRIA, <sup>2</sup>Department of Neurology, University of Tübingen, Tübingen, GERMANY, <sup>3</sup>Department of Neurology, University of Düsseldorf, Düsseldorf, GERMANY

Mitoxantrone is an anti-neoplastic anthracenedione derivative successfully used as an immunosuppressive agent in severe forms of multiple sclerosis (MS). Additional immunomodulatory effects have been suggested. In this study, we analysed the immunological effects of mitoxantrone in vitro.

Peripheral blood lymphocytes (PBL) from untreated or interferon-beta-treated MS patients or from healthy donors were stimulated in the presence or absence of mitoxantrone. B cells were isolated from PBL using monoclonal antibody-coated paramagnetic beads. Monocytes were enriched from PBL using their adhesion properties. Dendritic cells were cultured from monocytes. T-cell lines (TCL) reactive against tetanus toxoid (TT) were stimulated with TT on antigen-presenting cells. We analysed proliferation, cytokine production by intracellular immunofluorescence, and surface expression of activation markers, adhesion molecules and chemokine receptors. The mechanisms of cell death were analysed using annexin-V and DNA degradation detection systems.

Irrespective of the source of the PBL, mitoxantrone inhibited proliferation of activated PBL, B cells or TT-reactive TCL in a dose-dependent manner. In T and B-lymphocytes, surface expression of activation markers and cytokine production was not influenced substantially by mitoxantrone. In contrast, in monocytes and dendritic cells, mitoxantrone interfered with the antigen-presenting capabilities. Furthermore, Mitoxantrone induced apoptosis of B cells, monocytes and dendritic cells at low concentrations, whereas higher doses caused cell lysis.

We conclude that the beneficial effects of mitoxantrone in MS result (i) from its immunosuppressive potential based on non-specific cytotoxic effects on lymphocytes, (ii) from predominantly targeting monocytes and dendritic cells as major sources of antigen-presenting cells by inducing programmed cell death.

## P 2083

**Long-term expression patterns of cell surface bound and soluble adhesion molecules during interferon- $\beta$ 1b treatment in multiple sclerosis patients**

J. Kraus<sup>1</sup>, R. Bauer<sup>1</sup>, N. Chatzimanolis<sup>1</sup>, B. Engelhardt<sup>2</sup>, J. Tofighi<sup>1</sup>, T. Bregenzer<sup>3</sup>, B. S. Kuehne<sup>1</sup>, C. Laske<sup>1</sup>, E. Stolz<sup>1</sup>, F. Blaes<sup>1</sup>, K. Morgen<sup>1</sup>, H. Traupe<sup>1</sup>, M. Kaps<sup>1</sup>, P. Oschmann<sup>1</sup>  
<sup>1</sup>Justus-Liebig University, Giessen, GERMANY, <sup>2</sup>Max-Planck Institute, Bad Nauheim, GERMANY, <sup>3</sup>Parexel (biomat), Berlin, GERMANY

**Introduction** Adhesion molecules (AM) have been suggested to regulate the transmigration of leukocytes across the blood-brain-barrier (BBB), which is an essential step in the pathogenesis of multiple sclerosis (MS). In former studies, only the changes of the soluble forms of the adhesion molecules ICAM-1 and VCAM-1 have been serially investigated under treatment with interferon- $\beta$ 1b (IFN- $\beta$ 1b) in MS patients.

**Methods** 68 patients with relapsing-remitting MS were enrolled in this open study. 30 patients were treated with IFN- $\beta$ 1b, whereas 38 patients decided for themselves against immunomodulatory treatment. Blood was taken and detailed clinical examination was performed every three months, whereas brain MRI was assessed every six months for an observation period of 18 months. The expression levels of cICAM-1 and cICAM-3 on peripheral blood MNC were measured by two colors flow cytometry analysis. ELISA determined the soluble forms of VCAM-1, ICAM-1 and ICAM-3.

**Results** We found a short-term induction effect on the serum concentration levels of sICAM-1 and sVCAM-1 after three months of IFN- $\beta$ 1b treatment in MS patients. However, the expression levels of cell surface bound AM on blood MNC remained stable at the levels before treatment in the treated patients, whereas the untreated MS patients showed a continuously decreasing course in the expression of cell surface bound AM expression over 18 months.

**Conclusion** It can be speculated, that the stabilization of the BBB is one of the beneficial effects of IFN- $\beta$ 1b therapy in MS patients.

## P 2084

**Biochemical changes and cognitive function: Exploring sensitive markers in early stages of multiple sclerosis**

W. Staffen<sup>1</sup>, H. Zauner<sup>2</sup>, A. Mair<sup>1</sup>, A. Kutzelnigg<sup>1</sup>, H. Niederhofer<sup>1</sup>, G. Ladurner<sup>1</sup>, P. Kapeller<sup>3</sup>

<sup>1</sup>Christian Doppler Klinik, Salzburg, AUSTRIA,

<sup>2</sup>Rehabilitation Center Großgmain, Großgmain, AUSTRIA,

<sup>3</sup>University Graz, Graz, AUSTRIA

**Aim** of this study was to investigate cognitive function in relation to biochemical changes in corresponding brain areas of MS patients.

**Methods** 21 patients with relapsing-remitting MS, all within three year of disease duration and 21 age, sex and education matched controls were investigated. A psychometric assessment consisting of Wechsler Memory Scale (WMS) and the Multiple Sclerosis Functional Composite Score (MSFC) as well as a proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) examination of frontal white matter and the frontal part of cingulate gyrus (Area 32) were performed.

**Results** A significant reduction of the N-acetyl-aspartate (NAA)/Creatine (Cr) ratio in the frontal cingulate gyrus of MS patients was detected in comparison to controls. A significant drop of NAA/Cr ratio also was found in volumes positioned in cerebral white matter of MS patients including normal appear-

ing white matter (NAWM) and plaques. No NAA-changes were found in NAWM. With regard to psychometric results, the WMS general memory score showed significant statistical differences between patients and controls, whereas differences in MSFC results did not reach statistical significance. Regression analysis showed gray matter NAA/Cr ratio of the frontal cingulate gyrus as a significant predictor of distinct memory functions.

**Conclusions** We conclude that <sup>1</sup>H-MRS of gray matter in early stages of relapsing-remitting MS could be more sensitive in detecting early metabolic disturbances than <sup>1</sup>H-MRS of white matter, particularly in subjects without or with minor clinical impairment and in the absence of plaques in routine MRI.

## P 2085

**Comparative study of different brain MTR parameters for the study of multiple sclerosis**

Y. M. Zhui<sup>1</sup>, J. Grimaud<sup>1,3</sup>, L. Q. Zhou<sup>1</sup>, M. Filippi<sup>4</sup>, M. Rovaris<sup>4</sup>

<sup>1</sup>CREATIS, Villeurbanne, FRANCE, <sup>2</sup>Hospital of Neurology of Lyon, Lyon, FRANCE, <sup>3</sup>Hôpital Fontenoy, Chartres, FRANCE,

<sup>4</sup>Neuroimaging Research Unit, Department of Neuroscience, Scientific Institute Ospedale San Raffaele, Milan, ITALY

Parameters from magnetic transfer ratio (MTR) have been used to assess multiple sclerosis (MS) disease burdens, predict patients' clinical disability, and study different stages of lesion pathology and pathological evolution in MS patients. This study aims to quantify, in a systematic manner, the behaviours of these different MTR parameters in the context of MS study.

Eight parameters have been calculated. All the MTR parameters consistently showed a smaller value in the MS patients group than in the normal controls group. However, only global MTR, mean MTR, MTR25 and AMTR2/3 presented a significant difference between the MS patients and normal controls groups, with more or less important relative differences. In particular, the parameter AMTR2/3 presented the greatest discriminating ability. When applying the MTR parameters to the two normal controls groups from two different imagers, all the parameters exhibited different values in these two groups cases. But, the variation of the parameter AMTR2/3 was about 5%, and it was not significant; the variation of other MTR parameters was significant, and always more than 20%. In terms of mean, standard deviation and standard deviation to mean ratio, the parameter peak height presented the greatest variability. The other parameters had relatively close variability's. So, the parameter AMTR2/3 was less sensitive to change of imagers than the other MTR parameters while keeping a good ability of discriminating the MS patients and normal controls groups. In conclusion, the MTR histogram parameter AMTR2/3 offers the best compromise between increasing the discriminating ability and reducing variability.

## P 2086

**A structural, metabolic and functional MRI study in patients at presentation with clinically isolated syndromes suggestive of MS**

M. Filippi<sup>1</sup>, M. A. Rocca<sup>1</sup>, D. Mezzapesa<sup>1</sup>, A. Ghezzi<sup>2</sup>, A. Falini<sup>1</sup>, V. Martinelli<sup>1</sup>, G. Scotti<sup>1</sup>, G. Comi<sup>1</sup>

<sup>1</sup>Ospedale San Raffaele, Milan, ITALY, <sup>2</sup>Ospedale di Gallarate, Gallarate, ITALY

Recent MRI and pathologic studies have demonstrated the presence of axonal loss and dysfunction even in the early stages of multiple sclerosis (MS). In this study, we used functional



magnetic resonance imaging (fMRI) to assess the brain pattern of movement-associated cortical activations in patients at presentation with clinically isolated syndromes (CIS) suggestive of MS. To obtain additional information about the role and pathological basis of cortical plasticity in these patients, we also obtained conventional and diffusion tensor (DT) MRI scans of the brain as well as we measured N-acetylaspartate (NAA) concentration of the whole brain and correlated these measures with the extent of brain activations.

From 16 right-handed patients at presentation with CIS and 15 controls, we obtained: a) fMRI (repetitive flexion-extension of the last four fingers of the right hand), b) dual-echo scans, c) pulsed-gradient spin-echo echo-planar sequence to calculate DT-MRI maps, d) 1H-MR spectroscopy sequence to assess whole brain NAA levels.

Compared to controls, patients with CIS had significantly different DT-MRI metrics of the normal-appearing brain tissue and a decreased NAA levels. They also had more significant activation of the contralateral primary somatomotor cortex (SMC), secondary somatosensory cortex, inferior frontal gyrus and cerebellar hemisphere. Relative activation of the contra lateral primary SMC was correlated with T2 lesion volume and whole brain NAA levels.

This study demonstrates that functional cortical changes can be detected in patients at presentation with CIS. These changes might have a favourable role in limiting the impact of sub cortical white matter damage on subsequent disease evolution.

#### P 2087

##### **Changes of peripheral blood immune phenotypes including interleukin-expressing cells in multiple sclerosis patients, during two-year IFN- $\beta$ -1a therapy. A flow cytometry analysis.**

D. Mirowska<sup>1,2</sup>, A. Paz<sup>2</sup>, J. Skierski<sup>3</sup>, J. Zaborski<sup>1</sup>, M. Koronkiewicz<sup>3</sup>, J. Kruszezewska<sup>1</sup>, A. Czlonkowski<sup>2</sup>, A. Czlonkowska<sup>1,2</sup>

<sup>1</sup>Institute of Psychiatry and Neurology, Warsaw, POLAND,

<sup>2</sup>Department of Experimental and Clinical Pharmacology, Medical University, Warsaw, POLAND, <sup>3</sup>Laboratory of Flow Cytometry, Drug Institute, Warsaw, POLAND

**Introduction** "Peripheral hypothesis" of multiple sclerosis (MS) attributes its origin to an immune-mediated process based on peripheral reactivation of myelin-specific T cells. IFN- $\beta$ -1a treatment has shown to be a beneficial in MS but the primary mechanism responsible for its therapeutic influence remains unclear. Possible IFN- $\beta$ -1a action might be due to a regulatory effect on the immune system.

**Method** We have studied 20 outpatients with a relapsing-remitting form of MS treated with IFN- $\beta$ -1a for 24 months. Using two-colour flow cytometry we have determined the following immunologic cells phenotypes: CD3+CD19-, CD3-CD19+, CD3+CD8+, CD3+CD4+, CD3-CD16+56+, CD3+CD25+, CD19+CD25+, CD14+CD25+, CD14+CD86+, CD19+CD80+ before treatment, after 6, 9, 12 and 24 months of therapy. Cells producing cytokines: CD3+IL-10, CD14+IL-10, CD3+IL-4, CD3+IFN- $\gamma$ , CD14+IL-12 were measured before IFN- $\beta$ -1a administration, after 12 and 24 months of treatment.

**Results** In MS patients an increased percentage of CD3+CD25+ and CD14+CD86+ cells were noticed after 6, 9 and 12 months of therapy. Among cytokines producing cells, we observed an increased fraction of CD3+IL-4, which persisted to a lower extent (over 24 month-treatment.) In turn, an increased percentage of CD14+IL-10 cells observed after 12 month, decreased after 24 months of IFN- $\beta$ -1a administration.

**Conclusions** The beneficial effect of IFN- $\beta$ -1a was well seen during the whole study but was most evident after the first year of treatment.

Activated T cells may represent Th2 subpopulation, which release anti-inflammatory cytokines (e.g. IL-4). They act as antagonists to Th1 pro-inflammatory cytokines, possibly leading to limitation of the myelin sheet damage which results from inflammation ongoing in the brain.

#### P 2088

##### **Molecular determination of human herpes virus 6 (hhv-6) in serum and CSF of patients with multiple sclerosis (MS)**

U. Aguglia<sup>1</sup>, C. Russo<sup>1</sup>, F. Morabito<sup>1</sup>, M. Cuzzola<sup>2</sup>,

A. Cuzzocrea<sup>2</sup>, O. Iacopino<sup>2</sup>, P. Iacopino<sup>2</sup>

<sup>1</sup>CRE Neurologia, Reggio Cal., ITALY, <sup>2</sup>CTMO, Reggio Calabria, ITALY

**Background** Different studies found high prevalence of human herpes virus type 6 (HHV-6)-specific IgM antibodies or HHV-6 DNA in serum of patients with multiple sclerosis (MS). No control groups were included in these studies.

**Aim of the study** Prevalence of HHV-6 DNA in serum and cerebro-spinal fluid (CSF) of both MS-patients and control subjects.

**Patients and methods** Serum and CSF were obtained from 52 patients with MS and in 52 control subjects with no evidence of neurological disease. HHV-6 DNA was analysed by nested-PCR, amplified region ORF-U31.

**Results** All CSF and serum samples from controls were negative for HHV-6 DNA. HHV-6 DNA was detected in 9/52 (17%) serum samples and in 22/52 (43%) CSF samples from MS patients.

**Conclusion** These data support a potential pathogenetic role of HHV-6 in MS.

#### P 2089

##### **Long-term survey of cytokine production in secondary progressive multiple sclerosis**

D. Reske<sup>1</sup>, H. F. Peterreit<sup>1</sup>, O. R. Hommes<sup>2</sup>, W. D. Heiss<sup>1</sup>

<sup>1</sup>University of Cologne, Cologne, GERMANY, <sup>2</sup>European Charcot Foundation, Nijmegen, NETHERLANDS

**Introduction** Previous studies found a different cytokine profile in secondary progressive multiple sclerosis (SPMS) in comparison to healthy controls indicating an abnormal T-helper (Th) cell function in SPMS. Most studies are carried out as cross-sectional analyses. Hence, little is known about the evolution of cytokine production in SPMS. Here we report a follow-up of cytokine production in SPMS.

**Methods** In 34 patients with definite multiple sclerosis (MS) according to the Poser criteria and secondary progressive course of the disease the EDSS was measured before start of treatment and every three months during the 12 months observation period. Additionally, the production of IFG, TNF and IL10 in peripheral blood lymphocytes was measured at study entry and after 12 months of follow-up by flowcytometry.

**Results** Consistent with previous findings the pro-inflammatory cytokines IFG and TNF were significantly elevated in SPMS compared to healthy controls (p=0.001 respectively p<0.001, Mann-Whitney-test). Interestingly, IL10 failed to show any differences between both groups. Concurrent with the usual course of SPMS, the EDSS increased significantly from 5.1 to 5.5 within 12 months (p=0.023, Wilcoxon test). Additionally, the production of the two pro-inflammatory cytokines IFG (p=0.039) and TNF (p=0.01) increased significantly

during the follow-up. In contrast, the production of IL10 did not change significantly during the observation period.

**Conclusion** Confirming previous results, SPMS is accompanied with enhanced production of pro-inflammatory cytokines in comparison to healthy controls. Furthermore, enhanced pro-inflammatory cytokines tend to increase over time as does the disability measure EDSS.

#### P 2090

##### **Clinical and laboratory data in 7 cases of acute disseminated encephalomyelitis**

C. F. G. Redant, S. Goffette, A. Jeanjean, A. Peeters, T. Duprez, C. J. M. Sindic

*Cliniques Universitaires Saint-Luc, Brussels, BELGIUM*

**Introduction** Acute disseminated encephalomyelitis (ADEM) is reported to be rare in adults and raises diagnostic problems with Multiple Sclerosis and primary infections of the CNS.

**Clinical data** We report a series of 7 patients (6 males, 1 female, age 17–60) presenting acute neurological disorder within three weeks after an upper respiratory infection (N=4), a flu-like syndrome (N=2), and a gastro-enteritis (N=1). Neurological signs and symptoms were due to transverse myelitis (N=2), cerebellitis (N=2), rhombencephalitis (N=1) and encephalitis (N=2). Seizures and bilateral frontal lobes involvement in the first one, aphasia and coma in the second one characterized the two latter cases. Four patients were treated by high dose of intravenous methylprednisolone. Recovery was complete in three cases and partial in four, but most daily activities were possible. Laboratory and MRI date: CSF was normal in only one case; pleocytosis was detectable in 4 cases and CSF-restricted oligoclonal IgG bands were always absent. EEG was performed in 4 cases and was abnormal in 3. Brain and/or spinal cord MRI was normal in 3 cases and showed lesions corresponding to neurological signs in 4. The infectious causal agent was determined in 5 cases (Parvovirus B19, Epstein Barr virus, Cytomegalovirus, Chlamydia pneumoniae and Mycoplasma pneumoniae).

**Conclusion** We stress the monophasic course of ADEM, the absence of oligoclonal IgG bands in the CSF, the absence of MRI lesions in three cases and the overall good outcome of these patients.

#### P 2091

##### **TNF-alpha up regulates chemokines and chemokine receptors in the central nervous system.**

A.R. Glabinski<sup>1</sup>, B. Bielecki<sup>1</sup>, Y. Han<sup>2</sup>, K. Selmaj<sup>1</sup> and R.M. Ransohoff<sup>2</sup>

<sup>1</sup>Department of Neurology, Medical University of Lodz, Lodz, POLAND, <sup>2</sup>Department of Neurosciences, Cleveland Clinic Foundation, Cleveland, OH, USA

Recent data suggest that the key players in the mechanism of inflammatory cell accumulation in the central nervous system (CNS) during multiple sclerosis (MS) are chemoattractant cytokines – chemokines. The mechanism leading to upregulation of chemokine system in the CNS is still under investigation. Our main goal is to identify factors upregulating chemokines and chemokine receptors in the inflamed CNS. Potential candidates for this role are proinflammatory cytokines, especially tumour necrosis factor -alpha (TNF-alpha).

**Methods** In this study chemokine and chemokine receptor expression was analysed *in vivo* in mouse brain after stereotaxic injection of TNF-alpha as well as *in vitro* in astrocytic culture stimulated with TNF-alpha. Gene expression was quantitated with RNase Protection Assay (RPA).

**Results** We detected increased expression of chemokines RANTES, monocyte inflammatory protein-1alpha (MIP-1alpha), MIP-1beta and MIP-2 as well as chemokine receptors CCR1, CCR2 and CCR5 in the brain shortly after intracerebral, stereotaxic injection of TNF-alpha. Cultured astrocytes stimulated *in vivo* with TNF-alpha expressed chemokines RANTES, MIP-1alpha, monocyte chemoattractant protein -1 (MCP-1), gamma-interferon-inducible protein-10 (IP-10) and chemokine receptors CCR1 and CCR5.

**Conclusions** Our results confirm that proinflammatory cytokine TNF-alpha may upregulate chemokines and chemokine receptors in the brain and may contribute to development of neuroinflammatory disorders like MS.

#### P 2092

##### **Intrathecal IgG synthesis: indicator of progression in multiple sclerosis patients**

V. A. Daskalovska, Z. Z. Daskalovski, T. Boskova-Petkova  
*Clinic of Neurology, Skopje, MACEDONIA*

**Objectives** We studied the power of IgG synthesis value as an indicator of disease activity in multiple sclerosis (MS).

**Material and methods** Link index (LI) and modifiable Schüller formula (MSF) was used in 100 MS patients. Time between first, second and third attack and progression index (PI) were compared in patient with normal, high and very high Link index and value of intrathecal IgG calculated with modifiable Schüller formula.

**Results** Secondary progressive (SP) patients had a higher LI and MSF than relapsing-remitting (RR) and primary progressive (PP) courses (1.07 plus minus 0.5 for SP vs. 0.78 plus minus 0.5 for RR and 0.79 plus minus 0.5 for PP, P=0.01 and 0.03, respectively). Having a high index and high level of IgG with MSF in MS RR and SP patients has no time effect in the development of the second and third attack. PI was higher in patients with very high LI and with high level of IgG with MSF vs. patients with normal LI and normal level of IgG with MSF and high LI and high level of intrathecal IgG synthesis.

**Conclusions** This study confirmed that LI and formulas for determination of intrathecal IgG synthesis is a good marker of subsequent progression of MS.

#### P 2093

##### **Electrophysiological assessment of cognitive disturbances in patients with multiple sclerosis (study by P300)**

A. Podlecka, M. Gawel, A. Karwanska, B. Zakrzewska-Pniewska

*Department of Neurology, Medical University, Warsaw, POLAND*

Electrophysiological tests (P300 cognitive potentials) as related to MRI and neuropsychological tests results are rarely studied in MS patients with cognitive dysfunction. Twenty-four patients with clinically defined MS in remission, 18 females and 6 males were examined with neuropsychological and paraclinical tests. The aim of the study was to evaluate the P300 results in MS patients and their relation to the neuropsychological tests and MRI results. The neuropsychological assessment consisted on MMSE examination as a screening test for dementia, Wechsler Adult Intelligence Scale-Revised (WAIS-R) Test (IQ) for verbal intelligence and Wisconsin Card Test for abstract reasoning testing. MS patients were frequently impaired on measures of concentration, sustained attention and immediate memory. P300

cognitive potentials (delay in latency or absence of response) correlated with the degree of MRI abnormalities – brain atrophy on MRI was more frequently found ( $p < 0.05$ ) in patients with lower values of IQ. According to our results P300 cognitive potentials abnormalities correlated with cognitive dysfunction and the degree of brain atrophy.

P 2094

**Intrathecal IgM synthesis as prognostic factor in multiple sclerosis (MS)**

L. M. Villar, J. Masjuan, C. M. C. Sádaba, J. F. Plaza, E. Roldán, P. González-Porqué, J. C. Alvarez-Cermeno  
*Hospital Ramon Y Cajal, Madrid, SPAIN*

**Introduction** We have recently reported that intrathecal IgM synthesis (ITMS) correlates with higher EDSS in MS. In the same study we found that ITMS is more frequent in patients with secondary progressive MS that in those with a relapsing-remitting course. The significance of intrathecal IgM in patients that are in the initial stages of the disease remains uncertain.

**Methods** We studied 22 laboratory supported MS (LSMS) patients. 21 patients showed a relapsing-remitting (RR) course and one a primary progressive (PP) form. The patients were followed for a variable period of time ranging from 6 to 36 months (mean=18.00±2.83 months). OGC IgM bands were performed by IEF. Samples were diluted in saline to avoid IgM precipitation and incubated with 50 mM DTT at pH 9.5 to reduce IgM. IEF was performed at pH 5–8 and an anti-human IgM labelled with alkaline phosphatase was used in the immunodetection.

**Results** The probability of remaining without a second relapse was 10% after eight months of follow up for patients with ITMS, and 48.8% after 36 months for patients without ITMS ( $p=0.0001$ ). Patients with ITMS suffered more relapses ( $2.00 \pm 0.50$ ) than those without ITMS ( $0.58 \pm 0.26$ ) ( $p=0.022$ ). At the end of the follow up period, differences were found between EDSS of patients with ITMS ( $1.70 \pm 0.23$ ) and patients without ITMS ( $0.79 \pm 0.22$ ) ( $p=0.02$ ).

**Conclusion** These data seem to indicate that ITMS is a prognostic factor in the initial stages of MS.

P 2095

**Correlations of clinical and immunological data with magnetic resonance imaging (MRI) parameters in patients with multiple sclerosis (MS)**

A. Ilves, I. Nikiforova, I. Stoliarov, A. Petrov  
*Institute of Human Brain, St.Petersburg, RUSSIAN FEDERATION*

**Introduction** MS is an inflammatory, demyelinating and neurodegenerative disease of central nervous system. At the present time the relationship between MRI data, clinical and immune status of MS patients is not clear.

**Objective** To compare clinical, immunological and MRI parameters in MS patients.

**Patients and methods** 12 patients with relapsing-remitting and 6 with secondary progressive MS aged 19 to 53 were observed. All patients were in a remissions phase. The duration of the disease was 2–14 years. Patients were assessed using the Kurtzke expanded disability status scale (EDSS) score as well as immunological and MRI examination. Immunological monitoring included the measurement concentration levels of IFN-g and lymphocyte sensitisation to myelin basic protein

(MBP) in peripheral blood. 20 healthy volunteers were served as a control group. T2-weighted MRI measured the number and volume of the lesions.

**Results** Number of lesions correlated with duration of the disease. There are no correlations between lesions volume and EDSS. However, lesions volume correlated positively with the number of exacerbation, concentration levels of IFN-g and lymphocyte sensitisation to MBP.

**Conclusion** We have demonstrated that degree of inflammatory immunological activities correlated with development of destructive lesions in the brain in MS patients. Our results suggest, that neuro-immunological interactions may play an important role in pathogenesis of disease.

P 2096

**MR spectroscopy in Balo's concentric sclerosis**

T. Berkowicz, M. Siger-Zajdel, K. Zaleski, A. Mochecka-Thoelke, K. W. Selmaj  
*Department of Neurology, Medical Academy of Lodz, Lodz, POLAND*

**Introduction** Balo's concentric sclerosis (BCS) is one of the rare variants of multiple sclerosis (MS) characterized pathologically by concentric lesions composed of rings of alternating demyelination and relatively spared myelin. BCS which was diagnosed usually post mortem now can be recognized by its characteristic magnetic resonance imaging (MRI) picture consist of irregular, concentric rings of increased signal on T2-weighted and contrast-enhanced on T1-weighted MRI images.

**Methods** Conventional brain MRI (1.5 T Siemens Magnetom Vision Plus) and MR spectroscopy (H-MRS) was performed in a case of BCS. Spectra were obtained by using stimulated echo acquisition mode (STEAM) [TR=6000 TE=20, 64 average].

**Results** Two typical concentric ring lesions and also few MS-like lesions were detected on conventional brain MRI. Results of H-MRS obtained from concentric lesion showed the reduction of NAA/Cr and NAA/Chol ratios and increase of Chol/Cr ratio compare to normal white matter with no wide lipid peak located at 0.9–1.5 ppm. There were no differences of metabolites ratios between normal white matter in patient and control group.

**Conclusions** H-MRS gives additional arguments that BCS is a variant of MS and can be diagnosed ante mortem using MRI techniques.

P 2097

**Cellular immunity in patients with multiple sclerosis**

S. Kotov<sup>1</sup>, S. Suchkov<sup>1</sup>, V. Misikov<sup>1</sup>, Y. Zubova<sup>1</sup>, O. Durova<sup>1</sup>, N. Gnuchev<sup>2</sup>, R. Stepanenko<sup>3</sup>, A. Gabibov<sup>4</sup>  
*<sup>1</sup>Moscow Regional Research Clinical Institute (MONIKI), Moscow, RUSSIAN FEDERATION, <sup>2</sup>Institute of Gene Biology of RAMS, Moscow, RUSSIAN FEDERATION, <sup>3</sup>State Scientific Centre "Institute of Immunology", Moscow, RUSSIAN FEDERATION, <sup>4</sup>Institute of Bioorganic Chemistry of RAS, Moscow, RUSSIAN FEDERATION*

**Introduction** There are two types of multiple sclerosis (MS) courses remitting and progressing ones. The object of the study was to investigate cellular immunity typical for both MS types.

**Methods** A total of 28 MS patients were observed, 13 progressing type (PT), 15 remitting type (RT), 10 remissions, and 5 exacerbations. Lymphocyte CD+ subpopulations were studied using immunophenotyping method as well as their phagocytic function and natural toxicity (as compared with healthy donors).

**Results** In 2/3 of RT patients, CD3+ and CD8+ values decreased 1.5–2 times along with CD4/CD8 index increase by 10–30%; the values of CD25+, CD69+, and CD95+ increased 1.5, 2, and 3–5 times, correspondingly. In 11 of 13 PT patients, the values of CD3+, CD4+ and CD8+ decreased 1.5–2 times. The values of CD16+, CD20+, CD25+ and CD95+ didn't significantly differ from the control. None of the patients had any difference in CD5+, CD7+ and CD22+ values. CD95+ rise in RT patients correlate with amounts of CD16+, CD56+, CD19+, CD20+ and CD25+, bearing Fas (CD95)-ligand on their surface. Such a correlation wasn't noted in PT patients with decreased CD95+ value. The levels of CD16+ and CD56+ increased 8–12 times that correlated with natural cytotoxicity growth by 25–60%.

**Conclusion** Increased CD95+ level in the RT patients apparently reflects an activation of apoptosis having a defending function of both eliminating autoreactive T-killers and limiting the process of demyelination. Decrease of the general level of T-cells, T-helpers and T-killers/suppressors is characteristic for RT-type of MS.

#### P 2098

##### **Cerebrospinal fluid and serum interleukin-6 and its receptors levels in relapsing-remitting multiple sclerosis patients**

G. Horvat<sup>1</sup>, A. Vlacic<sup>2</sup>, I. Zadro<sup>2</sup>, S. Vukadin<sup>2</sup>, F. Culo<sup>1</sup>

<sup>1</sup>School of Medicine, University of Zagreb, Zagreb, CROATIA,

<sup>2</sup>General Hospital Sveti Duh, Department of Neurology, Zagreb, CROATIA

**Introduction** Interleukin-6 (IL-6) has recently been implicated in the pathogenesis of multiple sclerosis (MS), as it was found localized in MS lesions. The functional receptor for IL-6 is a complex of signal transducing subunit glycoprotein 130 (sgp130) and the ligand binding subunit gp80 (sIL-6R). They interact to mediate intracellular signalling.

The aim of this study was to measure IL-6 and its soluble receptors (sIL-6R and sgp130) in the cerebrospinal fluid (CSF) and serum from relapsing-remitting MS patients (RRMS).

**Patients and methods** We analysed CSF and serum samples of 21 RRMS patients during acute exacerbation of the disease, and 19 patients with noninflammatory neurological diseases (NIND), as controls. IL-6, sIL-6R and sgp130 levels were measured using enzymeimmuno test (ELISA). One-way ANOVA was applied for statistical analysis of the data.

**Results** Our preliminary results (mean±S.D. in pg/mL) showed statistically different serum IL-6 level in RRMS (27.79±61.33) and NIND (106.04±125.93) patients. However, there was no statistical difference between CSF IL-6 level in RRMS (2.90±2.68) and NIND (2.97±2.59) patients. Serum sIL-6R level was not statistically different between RRMS (25 795.55±8511.27) and NIND (21840.12±6379.43) patients, but CSF level were statistically different between RRMS (630.26±522.19) and NIND (159.84±273.41) group. Serum sgp130 levels were statistically different in RRMS (333750±88070) and NIND (415590±124160) patients. The CSF sgp130 level between RRMS (46710±26280) and NIND (54250±22560) group was not statistically different.

**Conclusion** Our preliminary results suggest that IL-6 and its soluble receptors (sIL-6R and sgp130) regulation may be altered in RRMS during acute exacerbation of the disease.

#### P 2099

##### **Relapsing optic neuritis: neurosyphilis, multiple sclerosis or both**

M. Monteiro, M. J. Rosas, F. Simões-Ribeiro, J. Castro-Neves, R. Vaz, M. J. Sá, M. E. Rio

Hospital S. João, Porto, PORTUGAL

**Introduction** Optic neuritis (ON) may be idiopathic or secondary to much different aetiology, the most common of which is multiple sclerosis (MS). Neurosyphilis can also cause ON due to vasculitic demyelination. Both disorders may have similar aspects in brain imaging and CSF studies play an important role in the differential diagnosis, although oligoclonal bands may be present both in MS and neurosyphilis. We present a case of bilateral relapsing-remitting ON in which the aetiology remains controversial.

**Case report** A Female, 44 years old; in 1999, she had several episodes of blurred vision in the right eye with progressive decrease in visual acuity. One year later, she had a transient episode of visual deficit on the left eye. Brain MRI (01/2001): several white matter lesions suggestive of inflammatory/demyelinating disorder. In June 2001 there was worsening of the visual acuity on the left, which improved only slightly with corticosteroids. Neurological examination: bilateral papillitis; low visual acuity; no other deficits. Positive VDRL, reactive TPHA; CSF: 124 cells, 70% lymphocytes; proteins: 0.6 g/dl; normal glucose; positive VDRL, reactive TPHA; oligoclonal bands positive in CSF, absent in serum. She was treated with penicillin, with slight improvement of the visual acuity. Brain spectroscopic MRI (three months later): demyelinating lesions highly suggestive of MS. She will repeat CSF studies.

**Conclusions** Although CSF tests are in favour of neurosyphilis, imaging tests still raise some doubt about the definitive diagnosis. This case exemplifies the difficulties in making the differential diagnosis between MS and MS-like conditions such as neurosyphilis, in monosymptomatic ON.

#### P 2100

##### **Quantitation of the specific and polyspecific intrathecal immune response in herpes simplex encephalitis, subacute sclerosing panencephalitis and multiple sclerosis**

C. Jacobi<sup>1</sup>, H. Reiber<sup>2</sup>

<sup>1</sup>University of Heidelberg, Heidelberg, GERMANY, <sup>2</sup>University of Göttingen, Göttingen, GERMANY

**Introduction** In acute diseases intrathecally synthesized antibodies against the causal antigen and in multiple sclerosis (MS) an intrathecal synthesis of measles, rubella and varicella-zoster virus (VZV) antibodies, the MRZ-antibody-reaction, as a part of the oligoclonal polyspecific immune response, can be measured.

**Methods** We measured the concentration of herpes simplex virus (HSV) antibodies in HSV encephalitis (n=4), measles antibodies in subacute sclerosing panencephalitis (SSPE) (n=5), of the MRZ-antibody-reaction in MS (n=65) and of measles, rubella, VZV and HSV antibodies in controls (n=25; except HSV antibodies, n=7) with an ELISA in cerebrospinal fluid and serum.

**Results** The concentration of intrathecally synthesized measles antibodies in SSPE is around 300-fold higher (median: 27.2 mg/l, range: 19.5–42.4 mg/l) than in MS-patients, who synthesize these antibodies intrathecally (median: 0.09 mg/l, range: 0.002–2.1 mg/l). The fraction of intrathecally synthesized virus specific antibodies as part of the total intrathecally synthesized IgG is 18.8% (range 11.8–27.5%) in SSPE (measles antibodies)

and 8.8% (range: 3.5–12.5%) in HSV encephalitis (HSV antibodies). These results show that there is also a large polyspecific immune response in acute diseases.

The fraction of measles, rubella and VZV antibodies in MS is 0.52%, 0.53% and 0.23% (for all three median of 1.4%, maximum 7%).

**Conclusion** In conclusion, the concentration of intrathecally synthesized antibodies against the causal antigen has higher amounts (titers) and leads to a higher fraction of intrathecally synthesized specific antibodies than the polyspecific immune response in multiple sclerosis, but seems just to be a small part of the total intrathecal immune response.

#### P 2101

##### **Cerebrospinal fluid/serum nitrite and nitrate ratio correlates with blood brain barrier disruption in relapsing-remitting multiple sclerosis patients**

G. Toncevi<sup>1</sup>, G. Samardzic<sup>2</sup>, B. Milicic<sup>3</sup>, S. Perovic<sup>4</sup>, S. Toncevi<sup>1</sup>  
<sup>1</sup>Clinical Hospital Centre, Kragujevac, YUGOSLAVIA,  
<sup>2</sup>Laboratory of Immunology, Kragujevac, YUGOSLAVIA,  
<sup>3</sup>Institute for Medical Statistics and Informatics, Kragujevac, YUGOSLAVIA, <sup>4</sup>Healthy Centre, Kragujevac, YUGOSLAVIA

**Introduction** An increase of interest has been witnessed in the role that nitric oxide plays in inflammation, demyelination and axonal injury, and also in the role that nitric oxide plays in multiple sclerosis (MS).

**Methods** We compared levels of cerebrospinal fluid (CSF) and serum nitric oxide metabolites in 63 patients with relapsing-remitting MS to those in 15 patients with other inflammatory neurological diseases (OINDs) and those in 10 patients with non-inflammatory neurological diseases (NINDs). Nitric oxide metabolites (nitrites and nitrates) were measured by the nitrate reductase and Griess reaction methods.

**Results** The MS patients were found to have significantly higher CSF and serum nitrite and nitrate levels compared with OIND and NIND patients (mean±SD; CSF=10.04±1.68 μM vs. 9.56±1.33 μM vs. 8.7±1.57 μM, p<0.001, and serum=57.86±7.17 μM vs. 52.05±3.11 μM vs. 45.51±6.06 μM, p<0.001, respectively). The CSF/serum nitrate and nitrite ratio was significantly elevated in MS patients (p<0.01). The CSF/serum nitrate and nitrite ratio correlates with blood brain barrier disruption (p=0.002) and has a trend to correlate with clinical activity of MS (p=0.057).

**Conclusion** These results support the evidence that nitric oxide has been implicated in inflammatory processes and suggest that nitric oxide might be potential mediator of blood brain barrier break down in inflammatory disease of the central nervous system, such as MS.

#### P 2102

##### **Activated protein C resistance in multiple sclerosis**

G. Niederwieser<sup>1</sup>, R. M. Bonelli<sup>1</sup>, H. Sternad<sup>1</sup>, W. Buchinger<sup>1</sup>, J. J. Archelos<sup>2</sup>, P. Költringer<sup>1</sup>  
<sup>1</sup>Barmherzige Brüder Hospital, Graz, AUSTRIA, <sup>2</sup>Dept. of Neurology, Karl-Franzens University, Graz, AUSTRIA

**Introduction** Prothrombotic states may be heritable, acquired or mixed. Although factor V Leiden is the most common cause of inherited activated protein C (APC) resistance, other changes in haemostasis cause acquired APC resistance, e.g. increased plasma levels of factor VIII or the presence of antiphospholipid antibodies. Prevalence of inherited APC resistance is reported to be between 2 and 15%. There is no report concerning acquired APC resistance in MS patients.

**Methods** 65 patients (14 men) with definite relapsing-remitting MS (RRMS), without a history of thromboembolism in their families, were examined for a prothrombotic state. Serum samples were investigated for APC resistance, antithrombin III, protein C and S.

**Results** We found a prevalence of 9.23% (n=6) of pathologic APC resistance, whereas 11 patients were at the lowest normal limit. One female patient experienced deep vein thrombosis. Anticoagulation was initiated.

**Conclusion** Although there are no prevalence data for acquired pathologic APC resistance, the prevalence in our group of patients seems to be surprisingly high. This preliminary study should be the trigger for further investigations on APC resistance in MS patients.

#### P 2103

##### **Humoral immunity in patients with multiple sclerosis**

V. Misikov<sup>1</sup>, O. Pronina<sup>1</sup>, N. Gnuchev<sup>2</sup>, R. Stepanenko<sup>3</sup>, O. Durova<sup>1</sup>, A. Gabibov<sup>4</sup>, S. Suchkov<sup>1</sup>, S. Kotov<sup>1</sup>  
<sup>1</sup>Moscow Regional Research Clinical Institute (MONIKI), Moscow, RUSSIAN FEDERATION, <sup>2</sup>Institute of Gene Biology of RAMS, Moscow, RUSSIAN FEDERATION, <sup>3</sup>State Scientific Centre "Institute of Immunology", Moscow, RUSSIAN FEDERATION, <sup>4</sup>Institute of Bioorganic Chemistry of RAS, Moscow, RUSSIAN FEDERATION

#### P 2104

##### **Relations between the membrane-mediated lipid and immune disturbances in multiple sclerosis**

L. I. Sokolova<sup>1</sup>, N. N. Yurzhenko<sup>2</sup>  
<sup>1</sup>National Medical University, Kiev, UKRAINE, <sup>2</sup>National Medical University, Kiev, UKRAINE

## Neuro-oncology Neurotoxicology

#### P 2105

##### **Hu and VGCC antibodies related to the prognosis of small-cell lung cancer**

S. Monstad<sup>1</sup>, J. Aarseth<sup>1</sup>, A. Storstein<sup>1</sup>, L. Drivsholm<sup>2</sup>, B. Lang<sup>3</sup>, A. Vincent<sup>3</sup>, C. Vedeler<sup>1</sup>  
<sup>1</sup>Haukeland Hospital, Bergen, NORWAY, <sup>2</sup>Department of Oncology and Haematology, Næstvedt Hospital, DENMARK, <sup>3</sup>John Radcliffe Hospital, Oxford, UNITED KINGDOM

**Introduction** Hu antibodies have previously been associated with longer survival of patients with small-cell lung cancer (SCLC). VGCC antibodies play a pathogenic role in the Lambert Eaton myasthenic syndrome (LEMS) which is also associated with SCLC, and these antibodies may reduce tumour growth. We tested a large cohort of sera from SCLC patients to see whether Hu and VGCC antibodies correlated with better SCLC prognosis.

**Method** 200 patients with SCLC (age 39–79, mean 62.3 years; 129 males and 71 females) receiving similar treatment were studied. Sera from these patients were examined for Hu antibodies by an immunoprecipitation assay and by immunohistoche-

mistry/Western blot. VGCC (P/Q subtype) antibodies were detected by radioimmunoassay. Survival analysis was used to evaluate the data.

**Results** Hu antibodies were detected in 51/200 (25.5%) by immunoprecipitation and 37/200 (18.5%) by immunohistochemistry/Western blot, whereas VGCC antibodies were detected in only 10/200 (5%) of the patients. Hu antibodies did not correlate with VGCC antibodies, and there was no association between Hu or VGCC antibodies and the extent of the disease, metastatic sites or survival.

**Conclusion** Hu and VGCC antibodies are found in a proportion of SCLC patients, but their presence does not correlate with the prognosis of the SCLC, and they probably do not suppress tumour growth.

#### P 2106

##### **Pyramidal cell antibodies associated with limbic encephalitis and thymoma**

A. Knudsen<sup>1</sup>, A. Storstein<sup>1</sup>, L. Oltedal<sup>2</sup>, S. Davanger<sup>2</sup>, C. A. Vedeler<sup>1</sup>

<sup>1</sup>Haukeland Hospital, Bergen, NORWAY, <sup>2</sup>University of Bergen, Bergen, NORWAY

**Introduction** Paraneoplastic neurological syndromes are rare, but very disabling neurological diseases that arise as remote effects of several different tumours. Thymoma can be associated with various antibodies such as anti-AChR, anti-titin, anti-RyR, anti-VGKC and anti-CV2. We report a new paraneoplastic antibody that may be related to thymoma.

**Methods** A 52-year-old patient developed limbic encephalitis with focal epileptic seizures. Screening for occult cancer revealed a thymoma. Paraneoplastic antibodies related to limbic encephalitis such as anti-Hu, anti-amphiphysin, anti-Ta, anti-CV2, anti-Ri and those related to thymoma as mentioned above were negative. Serum from this patient and from 10 patients with thymoma and myasthenia gravis were examined for antibodies against hippocampal antigens by immunohistochemical methods.

**Results** Serum from the patient with limbic encephalitis and thymoma stained hippocampus from rat brain. Furthermore, confocal immunofluorescence studies showed that axonal boutons and growth cones of hippocampal neurons in culture were distinctly labelled, colocalizing with the vesicle marker synaptophysin. Western blot of rat brain extract revealed a band of approximately 60 kDa. Such antibodies were not detected in the sera from 10 other patients with thymoma.

**Discussion** We describe a new possible paraneoplastic antibody against pyramidal cells that may be associated with limbic encephalitis and thymoma.

#### P 2107

##### **Inhibition of human glioma cell growth by a PHS-2 inhibitor, NS398, and a prostaglandin E receptor subtype EP1 selective antagonist, SC51089**

M. Matsuo, N. Yoshida, M. Zaito, Y. Hamasaki  
Saga Medical School, Saga, JAPAN

**Introduction** Prostaglandin H synthase (PHS) is a key enzyme in the synthesis of prostaglandins (PGs). Recently, enhanced expression of PHS-2 in brain tumours and its correlation to the histopathological grade of glioma has been reported. Furthermore, *in vitro* inhibition of growth of glioma cells by a specific PHS-2 inhibitor, NS398 has been demonstrated. It was also

shown that PGE<sub>2</sub> contribute colon carcinogenesis through its binding to the prostaglandin E receptor subtype EP1. We therefore evaluated the effect of a specific PHS-2 inhibitor, NS398, and EP1 antagonists, SC51089 and AH6809, on glioma cell lines.

**Methods** Two glioma cell lines, one is PHS-2 positive cell line (KMG4) and the other is PHS-2 deficient cell line (A172), were used. To evaluate anchorage-dependent growth, 5-Bromo-2'-deoxy-uridine (BrdU) labelling and detection kit III (Boehringer Mannheim) was used, while colony forming assay was used for anchorage-independent growth. *In vivo* tumour growth was assessed using KMG4 tumour xenografts on SCID mice.

**Results** NS398 inhibited anchorage-dependent and -independent growth of glioma cell lines regardless of PHS-2 expression, suggesting there are some PHS-2 independent mechanisms for antineoplastic effect of NS398. However, the antineoplastic effect was attenuated by addition of PGE<sub>2</sub>, which is one of the main products of PHS, suggesting that the predominant mechanism is PHS dependent. EP1 antagonists, SC51089 and AH6809, inhibited the growth of glioma cell lines *in vitro*. Furthermore, NS398 or SC51089 slowed tumour growth *in vivo*.

**Conclusion** PHS-2 inhibitors and EP1 antagonists might be useful in the prevention and/or treatment of glioma.

#### P 2108

##### **Changes in EEG photic driving in workers exposed to mercury vapours**

P. Urban<sup>1</sup>, E. Lukáš<sup>1</sup>, J. Nerudová<sup>1</sup>, V. Krajca<sup>2</sup>, Z. Cábeková<sup>3</sup>, M. Cikrt<sup>1</sup>

<sup>1</sup>National Institute of Public Health, Praha, CZECH REPUBLIC, <sup>2</sup>Faculty Hospital Bulovka, Praha, CZECH REPUBLIC, <sup>3</sup>3rd Faculty of Medicine, Charles University, Praha, CZECH REPUBLIC

**Objective** To study photic driving (PD) in workers exposed to mercury.

**Subjects and methods** 24 workers from a chloralkali plant exposed to mercury (mean age 42 yrs, mean duration of exposure 15 yrs); 24 matched controls. Mean air-borne concentration of Hg at workplace 59 µg/m<sup>3</sup>. Mean urinary excretion of Hg 64.3 µg/24 hours spontaneously, and 751.9 µg/48 hours after mobilization by sodium 2,3-dimercapto-1-propan sulfonate. Photic stimulation included frequencies 1–30 Hz.

**Results** The number of stimulation frequencies eliciting PD was higher in the exposed group, compared to the controls (median 17 and 10 frequencies, respectively; p<0.001). The maximum value of PD was higher in the exposed than in the control group (median 24.6 and 9.4 z-units, respectively; p<0.001). The median stimulation frequency with maximum driving was 15 Hz in the controls and 20 Hz in the exposed (p<0.01). The median sum of PD and the median index of PD were higher in the exposed than in the controls (p<0.01). The increased PD was mainly at high stimulation frequencies. There was no significant association between PD and exposure.

**Conclusion** PD is generated in the visual cortex. Mercury shows predilection for this structure. An increased PD is regarded as a sign of nervous system hyperexcitability (e.g. in migraine). Consequently, the increased PD in exposure to Hg could be interpreted as a marker of neuronal hyperexcitability due to an early neurotoxic effect of Hg.

**Acknowledgment:** The study was supported by grants IGA 5153-3, 4510/3, and NE/6222-3.

P 2109

**Neurological and neurophysiological examinations of workers occupationally exposed to aluminium.**

Halina Sinczuk-Walczak, Grazyna Razniewska,

Wanda Matczak

*Nofer Institute of Occupational Medicine, Lodz, POLAND*

**Introduction** Numerous studies are conducted to assess aluminium (Al) -induced toxicity to humans and environment. It has been implicated in the aetiology of Alzheimer's disease and other neurodegenerative disorders, though it is controversial. The aim of the present study was to assess the effects of aluminium on the functions of the nervous system in workers chronically exposed to this metal.

**Methods** The study covered a selected group of 67 male workers (mean age 38.7+/-10.3) involved in the aluminium production. Their employment duration ranged between 2 to 33 yr (mean 14.6+/-8.9yr). Aluminium oxide (Al<sub>2</sub>O<sub>3</sub>) concentrations varied from 0.2 to 2 mg/m<sup>3</sup> (arithmetic mean - 0.40 mg/m<sup>3</sup>, geometric mean - 0.35 mg/m<sup>3</sup>, standard deviation - 0.29). The control group consisted of 57 men non-occupationally exposed to Al, matched by sex, age and work shift distribution.

**Results** Clinically, the headache, increased emotional irritability, concentration difficulties, sleeplessness and mood swings predominated among the disorders of the nervous system functions in workers chronically exposed to Al. The objective neurological examinations did not reveal organic lesions in the central or peripheral nervous system. Generalized and paroxysmal changes were most common recordings in the abnormal electroencephalography (EEG). Visual evoked potentials (VEP) examinations revealed abnormalities, primarily in the latency of the response evoked.

**Conclusion** The results of this study suggest that Al<sub>2</sub>O<sub>3</sub> exposure to concentrations within MAC values produce subclinical health effect in the nervous system.

P 2110

**Nervous system dysfunction among workers with long-term exposure to manganese**

H. Sinczuk-Walczak, M. Jakubowski, W. Matczak

*Nofer Institute of Occupational Medicine, Lodz, POLAND*

**Introduction** Manganese (Mn) affects primarily the nervous system. Cases of grave damages have not been reported, and neurological examinations are focused on detecting early symptoms. Aim of our study was to assess nervous system health effects in workers of the shipbuilding and electrotechnical industries exposed to manganese.

**Methods** Tests were performed on a group of male workers (welders and fitters), aged 20 to 56 years (mean 39.17+9.79 years). Period of employment ranged from 1 to 41 years, mean 17.5+10.8 years. Air Mn concentrations during welding ranged from 0.004 mg/m<sup>3</sup> to 2.67 mg/m<sup>3</sup>, and the MAC value of 0.3 mg/m<sup>3</sup> was exceeded in 36 subjects. Values of the cumulative dose index ranged between 0.28 and 35.5, mean 8.37+6.48. Control group comprised 62 non-exposed males matched for age and work shifts to the exposed group. Neurological examination included subjective and objective examinations of the nervous system, electroencephalographic (EEG) and visual evoked potential (VEP) evaluations.

**Results** Neurological symptoms noted in the exposed group comprised states of emotional arousal, impaired memory and concentration, excessive sleepiness during daytime, paraesthesia in the extremities. Neurological examinations did not reveal any systemic changes in the central nervous system for diagno-

sing clinical encephalopathy or neuropathy. Generalised and paroxysmal changes dominated among abnormal EEG records. VEP tests revealed abnormalities in the evoked response, which may point to visual neuron disorders.

**Conclusion** Our results suggest the exposure to manganese within, or slightly above, the MAC (arithmetic mean - 0.389 mg/m<sup>3</sup>, geometric mean 0.154 mg/m<sup>3</sup>) value causes sub-clinical health effects in the nervous system.

P 2111

**Electroencephalographic findings in adolescents with glue sniffing**

S. Demirkaya, R. Dundaroz, T. Turkbay, E. Eroglu, O. Vural

*GATA, Ankara, TURKEY*

**Introduction** There are many case reports on severe central nervous system (CNS) effects of toluene in glue sniffers. The aim of this study was examine the effects of toluene in glue sniffers on the EEG in search of a central neurological dysfunction.

**Methods** We were tested 17 boys who were glue sniffers. A brief history of every subject was taken, and general physical and neurological examinations were performed. They had no clinical findings of neurological disorders by the examination. Haematological parameters, serum liver enzyme activities, and renal values of all subjects were within normal limits. The EEGs were recorded when patients were awake in daytime.

**Results** The ages of the subjects ranged from 13 to 18 years (mean, 15.4 years). They had quit the habit at least one month ago (range 1 to 3 months, mean 2.3 months). The duration of the abuse before rehabilitation ranged from two to five years, with a mean of 3.1 years. The EEGs were normal in seven subjects. Abnormal EEG was observed in 58.8% (n=10) of all the subjects. Seven subjects had various focal and/or diffuse EEG abnormalities.

**Conclusions** The changes of EEG are a sensitive measure of the effects of toluene on the CNS. However, the EEG results are not homogeneous for toluene abusers in all studies, as well as in our study. Therefore, we suggest that EEG may be useful addition to other clinical, laboratory and radiological means of examining toluene affecting the nervous system.

P 2112

**Neurotoxicity of tributyltin in Sprague-Dawley rat brain**C. Soo Youn<sup>1</sup>, S. Chi Won<sup>1</sup>, O. Jae Ho<sup>1</sup>, P. Ki Sook<sup>1</sup>, P. Sung Gyu<sup>1</sup>, H. Jin Tae<sup>2</sup>, P. Chang Won<sup>1</sup>, J. Hae Kwan<sup>1</sup>, Y. Ki Hwa<sup>1</sup><sup>1</sup>Department of General Toxicology, National Institute of Toxicological Research, Seoul, REPUBLIC OF KOREA,<sup>2</sup>College of Pharmacy, Chungbuk National University, Cheongju, REPUBLIC OF KOREA

**Introduction** The organotins such as tributyltin (TBT) are used mainly in wood preservation, marine antifouling paints, disinfection of circulating industrial cooling waters. There were also some reports indicating that the exposure to organotin compounds causes epilepsy and amnesia in human and experimental animals. However, neurotoxic effect and its mechanism were not fully understood. Therefore, we investigated the neurotoxic effect and mechanism of TBT in SD rats.

**Methods** 8 week-old male SD rats were treated orally TBT (0, 1, 3, 5 mg/kg/day) for 7 days. And other groups were treated orally TBT (10mg/kg) for single dose. The locomotor activity and immunohistochemical changes were examined.

**Results** We found slightly body weight loss in the group of 3.5mg/kg/day treatment. The distance travelled of TBT treated rats were decreased but resting time was slightly increased in a

dose-dependent manner. The number of tyrosine hydroxylase immunoreactive (TH-IR) neurons in SN and VTA, and processes in the compacta part and reticulosa part of SN was slightly decreased of TBT-treated rats in a dose-dependent manner. However, COX-2 IR cell numbers were increased in a dose-dependent manner in same regions. The GABA and calmodulin-IR cell numbers in Purkinje cells of cerebellum of 3 and 5mg/kg/day TBT treated groups were decreased, and single dose TBT treated groups were also decreased in 1, 3, 5 day but increased in 2 week. However, COX-2 was not expressed in the Purkinje cells of cerebellum.

**Conclusions** The dopaminergic neuron has inflammatory pathway and the Purkinje cell has calcium mediated apoptosis pathway by TBT treatment.

#### P 2113

##### **Alcoholism: acute and chronic neurological complications in 420 patients**

F. Vecchio, E. Menegazzo, C. Fattorello S.  
*Department of Neurology, Mirano (Venice), ITALY*

**Objective** To evaluate type, incidence and severity of alcohol related neurological disturbances.

**Materials** We studied 420 patients (pts), 225 males and 195 females, mean age 48.8 years, with anamnestic history of alcohol abuse for more than five years. All pts were treated in Neurological Department in the last 10 years in acute intoxication phase or for chronic neurological complications. All pts underwent clinical examination, routine blood laboratory tests (including alcoholemia and ammonemia), EEG, EMG, brain CT scan, psychological interview, neuropsychological tests and hepatic echography.

**Results** 84 pts, 54 males and 30 females, had more epileptic generalized seizures. The EEG was normal in 300 pts, with diffuse abnormalities in 85 and focal abnormalities in 30. Brain CT scan showed evidence of brain atrophy in 175 cases, with neuropsychological tests indicative for dementia in 25 pts (15 males and 10 females). The EMG showed a sensory-motor polyneuropathy in 329 pts.

The pts treated for an acute abstinence syndrome were 79.5%; among these 20% presented generalized epileptic seizures and 27.3% delirium tremens. The pts that presented as chronic complication a sensory-motor polyneuropathy of various severity (78.3%) were affected also by behavioural disturbances in 10% of cases, by alcoholic dementia in 6%, by Korsakow syndrome in 1.2% and by hepatic encephalopathy in 15%.

**Conclusion** From our study emerges a high incidence of hospitalisation for acute and chronic alcohol correlated neurologic pathologies with the presence of severe biologic complications that cause an elevated social-sanitary cost of the alcoholism.

#### P 2114

##### **Excitatory effect of B-n-methylamino-L-aspartate on retzius nerve cells of the leech haemopsis sanguisuga**

S. N.J. Lopacic<sup>1</sup>, D. Cemerikic<sup>1</sup>, D. Pavlovic<sup>3</sup>, M. Wendt<sup>3</sup>, M. Grgurevic<sup>2</sup>, D. Ristanovic<sup>1</sup>, V. Nedeljkovic<sup>1</sup>

<sup>1</sup>Department of Pathophysiology, <sup>2</sup>Department of Physiology, Medical Faculty, Belgrade, YUGOSLAVIA, <sup>3</sup>Klinik und Poliklinik für Anaesthesie und Intensivmedizin, Ernst-Moritz-Arndt Universität, Greifswald, GERMANY

Excitatory amino acid B-n-methylamino-L-aspartate (BMAA) is present in the plant *Cycas circinalis*, which is used in food and medicine by the population of western pacific region. That EAA

has been implicated in the pathogenesis of human neurodegenerative disorder western pacific amiotrophic lateral sclerosis-parkinsonism-dementia complex (ALS/PDC). Since Retzius cells possess glutamate receptors, we investigated the effect of L-BMAA on these cells. Intracellular recordings were made using glass tube microelectrodes filled by 3M KCl, with resistance of 5–15 MΩ. In our experiments average value of resting membrane potential was 51.2±25.8 mV (n=5). Bath application of L-BMAA (obtained from Prof P.S. Spencer, Oregon Health Sciences University, Portland, USA) in concentration of 10<sup>-2</sup> mol/l during 3 min elicited depolarisation. Average value of that depolarisation was 12.0±6.1 mV (n=5). Our experiments indicate that L-BMAA has excitatory effect on Leech Retzius nerve cells. We compared this effect to the effects of β-N-oxalylamino-L-aspartate (L-BOAA) and L-Aspartate (L-Asp) from our previous experiments on the same experimental model (1), and concluded that the effect of 10<sup>-2</sup> mol/l L-BMAA is comparable to the effects of 10<sup>-2</sup> L-Asp and 5x10<sup>-5</sup> mol/l L-BOAA. This indicates that L-BMAA is similar in potency to L-Asp, and approximately 500 times less potent than L-BOAA in our experimental model.

##### **References**

Cemerikic D, Nedeljkovic V, Lopacic S, Dragovic S and Beleslin B (2001). Excitotoxicity of Lathyrus Sativus neurotoxin in Leech Retzius neurons. *Physiol Res* 50: 205–214.

#### P 2115

##### **Nitrile neurotoxicity as model of human neurodegenerative diseases**

E. Balbuena, A. Seoane, J. Llorens

*Department of Physiological Sciences, University of Barcelona, Hospitalet de Llobregat, SPAIN*

Nitriles are a large family of compounds, and humans are routinely exposed to both industrial and natural nitriles. Their toxic properties include acute lethality and osteolathyrisms. In addition, a number of nitriles have neurotoxic effects. However, these effects are not well understood, and the potential for neurotoxicity of nitriles as a class has not been established. 3,3'-Iminodipropionitrile (IDPN) has been mostly studied as an agent causing a neurofilamentous proximal axonopathy, as observed for ALS disease. However, IDPN neurotoxicity was first known to cause permanent alterations in motor behaviour, an effect that remained unexplained in the early 90's.

Current evidence from our research group indicates that IDPN mainly affects the sensory systems, including the retina and the cornea, the olfactory mucosa, and the auditory and vestibular sensory epithelia. The vestibular toxicity is particularly relevant because it offers an explanation for the effects of IDPN on motor behaviour and as model of aminoglycosidic antibiotics toxicity. This sensory toxicity is also caused by other nitriles, including allylnitrile and cis-crotononitrile. The neurofilamentous axonopathy has only been demonstrated for IDPN. Thus nitriles show overlapping but not identical neurotoxic properties, and many of these rely on the nitrile group and do not require neither two nitrile groups nor the imino group that are exclusive to the IDPN molecule. Likewise, there are some similarities between their effects *in vivo* and some human neurodegenerative diseases, like neuropathic ataxia or spastic paraparesis, and can be used as models for studying ototoxicity or dizziness, apart of their industrial exposure interest.



P 2116

**Successful therapy of oligodendroglioma seeding in the CNS by combined long-lasting intrathecal (i.th.) and systemic chemotherapy**P. Krauseneck, A. Kreller, H. Weber  
*Dept. of Neurology, Bamberg, GERMANY*

A female (28yrs) 1989 was operated upon a right frontal oligodendroglioma. Local relapses in 1992 and new, remote relapses in 8/1994 were successfully treated with stereotactic RT. 3 new local lesions were re-operated in 10/1995. After presentation in our institution we conducted 4 cycles of PCV until 7/1996 and the pt. stabilized till 2/1997 when again a right frontal relapse occurred being treated again by stereotactic seed. 4/1998 3 new remote recurrences were diagnosed in the left frontal and temporal cortex corresponding to CSF dissemination. Atypical cells were present in CSF. I.th. Ara-C was started combined with 5 cycles ACNU+VM26 and 11/1998 CR was achieved with negative CSF and C11-Methionin-PET. I.th. Ara-C was continued until 5/1999 amounting to 27 injections with a total dose of 1580mg. 7 months after discontinuation in 12/1999 2 new CSF born metastases occurred left frontal/insula. I.th. Ara-C was resumed (again 27 injections with 1140mg total dose) and 8 cycles Temozolomide administered resulting in a new CR (10/2000). A final relapse in 1/2001 was unresponsive to further chemotherapy and now after a total dose of 2840mg Ara-C i.th. in conjunction with the preceding therapies neurotoxic ataxia occurred and Ara-C was stopped. A slowly progressive cognitive, particular memory decline was seen in the last 2 years.

**Conclusion** It is important to differentiate multifocal/multiple gliomas from secondary parenchymatous involvement from meningeal metastases since additional intrathecal chemotherapy may be an effective treatment, and prophylaxis of further seeding. Long-lasting i.th. Ara-C treatment is possible without obvious neurotoxicity.

P 2117

**Multiple central nervous system amyloidomas**P. Vrentas<sup>1</sup>, V. Panayiotopoulou<sup>1</sup>, G. Kottas<sup>2</sup>, S. Lahanis<sup>3</sup>, S. Sameli<sup>1</sup>, G. Kontogeorgos<sup>3</sup>  
*<sup>1</sup>Tripolis Psychiatric Hospital, Tripolis, GREECE, <sup>2</sup>401Army Hospital, Athens, GREECE, <sup>3</sup>Athens General Hospital, Athens, GREECE*

**Introduction** Amyloidomas rarely involve the Central Nervous System (CNS) and they are unrelated to systemic amyloidosis. CNS lesions either solitary or multiple invariably involve white matter and to some extent adjacent choroid plexus. A definite diagnosis relies on histological appearance of amyloid.

**Methods** We describe history, clinical presentation and laboratory findings that led to the diagnosis of multiple CNS amyloidomas in a male patient.

**Results** A 30-year-old male with unremarkable past medical history had a first episode of focal seizure affecting right arm which generalized subsequently. On examination the patient was alert without any focal deficits. MRI of his brain showed four high signal enhancing lesions without mass effect. Routine blood tests, HIV test, immunofixation of proteins and Computerized Tomography of his thorax and abdomen were normal. Cerebrospinal fluid examination showed near normal results. Stereotactic biopsy of the lesion in the left thalamus with Congo-red stain showed extensive deposits of amyloid as well as deposits in vessel walls. Extensive work-up for systemic amyloidosis was negative. Neuropsychiatric assessment disclosed no mental or cognitive abnormalities. His seizures were

controlled with valproate 1500mg/day and the patient recovered uneventfully. Because of the sites of the lesions surgery was not recommended.

**Conclusion** Although amyloidomas of the CNS are rare they must be considered in the differential diagnosis when atypical solitary or multiple lesions appear in brain or spine imaging producing relatively chronic non-specific symptoms.

P 2118

**Cisplatin associated stroke in a patient with extragonadal seminoma**S. Oberndorfer<sup>1,2</sup>, J. Pont<sup>3</sup>, H. Lahrmann<sup>1</sup>, S. Urbanits<sup>1</sup>, B. Hess<sup>1</sup>, W. Grisold<sup>1</sup>*<sup>1</sup>Kaiser Franz Josef Hospital, Department Neurology, Vienna, AUSTRIA, <sup>2</sup>Luwig Boltzmann Institute for Neurooncology, Vienna, AUSTRIA, <sup>3</sup>Department Oncology, Kaiser Franz Josef Hospital, Vienna, AUSTRIA*

We report a 43 old male patient who presented with acute thrombosis of the right brachial artery and ischemic stroke of right hemisphere after cisplatin infusion. Few reports in the literature describe cerebrovascular events after cisplatin infusion. However, the causal relation between a cisplatin and thrombotic events remains uncertain.

In our patient, a seminoma was diagnosed three month ago. One course of chemotherapy with cisplatin and etoposide was already applied without any severe side effects. The patient responded very well to chemotherapy. One day after the second course, the patient suffered from thrombosis of the right brachial artery and had multiple emboli in the right hemisphere. Neurological examination found severe neuropsychological deficits, as well as a left-sided hemiplegia. No cardiac source of embolism, or abnormal intravascular coagulation was found. The only predisposed risk factor for thrombosis was cigarette smoking. Because of good tumour response, further courses of cisplatin-based chemotherapy are planned. In order to prevent further thrombotic events, high dose heparin was given during the course of chemotherapy.

Cerebrovascular events related to cisplatin are rare, but have already been reported in patients with seminoma. Cisplatin is highly effective drug, also in patients with seminoma and therefore widely used. Although, no definite explanation for the association of cisplatin infusion and ischemic stroke can be proposed, a relation seems likely. Our report therefore emphasises a possible causal relation between chemotherapy and ischemic stroke in patients with seminoma. We recommend heparin in patients with thrombotic complications following cisplatin infusion.

P 2119

**Clinical symptoms and prognostic factors in breast cancer-related meningeal metastases.**

H. Rudnicka, A. I. Jagiello-Gruszfeld, A. Niwinska, T. J. Pienkowski

*The Maria Skłodowska-Curie Memorial Cancer Centre and Institute, Warsaw, POLAND*

**Purpose** Meningitis carcinomatosa (MC) is an uncommon but aggressive complication of advanced breast cancer with increasing incidence, recently.

**Patients and methods** We reviewed 20 cases of MC caused by breast cancer at our clinic. The neurological symptoms, pre-treatment characteristics and the methods of MC treatment were analysed. The treatment consisted of intrathecal injection of 10 mg of methotrexate plus dexamethasone 4 mg, administered

weekly. 15 pts (75%) received systemic chemotherapy in parallel with intrathecal treatment and 2 pts (10%) – systemic hormonal treatment. The whole brain radiotherapy was performed additionally in fourteen (70%) pts.

**Results** The mean age at the time of diagnosis of MC was 45 years (range 29–70) and the median Karnofsky status was 50% (range 40–80%). The clinical symptoms at the time of diagnosis were headache (85%), nausea/vomiting (40%), confusion (30%), cerebellar signs (25%), paresis (25%) and pain in the thoraco-lumbar region (10%). Cancer cells in cerebrospinal fluid were detected in 100% of cases. Cerebrospinal fluid protein level was elevated in 70% of cases.

The mean of intrathecal treatment cycles was 6, (range 0–15 cycles).

The response was defined as clinical and laboratory improvement and was achieved in fourteen pts (70%). The median duration of survival was 112 days.

**Conclusion** Our observation suggests, how important prognostic factors in MC are: systemic chemotherapy, Karnofsky status at time the diagnosis of MC and the clinical response (reduction of headache and other symptoms) after the first 2–3 cycles of intrathecal infusion of methotrexate.

#### P 2120

##### **Paraneoplastic neurologic syndrome – a case of lymphoma B**

G. Sousa, P. Abreu, S. Vieira, M. J. Rosas, C. Neves  
*Department of Neurology, Hospital S.João, Porto, PORTUGAL*

**Background** Paraneoplastic neurological syndrome (PNS) is an unusual neurological disorder affecting patients with cancer. It's caused by complex non-metastatic, sometimes immune-mediated mechanisms and not by the tumour itself. We present a case of PNS that preceded the diagnosis of B-cell lymphoma.

**Clinical case** Female, 64-year-old, admitted 2 weeks before for paresis of IV cranial nerve, was readmitted with an insidious progressive distal and symmetrical sensory limb disturbance, anorexia and weight loss. On examination she had: IV cranial nerve paresis; impaired perception of vibration, pin and light touch with a stocking-and-glove distribution and absent tendon reflexes in lower limbs. Laboratory study showed slight pancytopenia, hepatic dysfunction, abnormal immunology and high CA-125. Liquor study was normal. Electromyography revealed focal mononeuropathies (essentially demyelinating) and the somatosensory-evoked potentials showed impairment of posterior columns. Pelvic imaging disclosed an ovarian cyst. An inflammatory aetiology was excluded and no systemic (including gynaecologic) tumour was found. Afterwards, she began painless jaundice, fever and dysphagia. Further study revealed severe pancytopenia and bone marrow biopsy showed lymphoma B. Quimiotherapy was initiated with clinical improvement.

**Conclusion** The PNS in this case was characterized by a cranial neuropathy and sensorimotor neuropathies that preceded a B-cell lymphoma. The clinical and laboratory findings (CA-125) misled our investigation towards a gynaecologic tumour when in fact it was primarily haematological. Nevertheless, the recognition of PNS is important because it may help avoiding unnecessary studies to determine the cause of neurological disturbances in cancer patients.

## Autonomic nervous system Clinical neurophysiology Critical care

#### P 2121

##### **Myocardial 123I-metaiodobenzylguanidine (MIBG) Scintigraphy for the assessment of cardiac sympathetic nervous dysfunction in diabetic patients**

J. Nunomura<sup>1</sup>, O. Uehara<sup>2</sup>, M. Baba<sup>3</sup>, M. Matsunaga<sup>3</sup>  
*<sup>1</sup>Department of Neurology, Municipal Kuroishi Hospital, Kuroishi, Aomori, JAPAN, <sup>2</sup>Department of Internal Medicine, Municipal Kuroishi Hospital, Kuroishi, Aomori, JAPAN, <sup>3</sup>Department of Neurology, Hirosaki University, Hirosaki, Aomori, JAPAN*

**Purpose** Although diabetic autonomic neuropathy constitutes serious complications, there are few methods for early detection of abnormalities. In this study, we conducted 123I-MIBG myocardial scintigraphy, which is currently applied as a test of cardiac sympathetic nerve function, on diabetic patients, and assessed its usefulness by comparing with the results of sympathetic skin response (SSR), which is a method for evaluating peripheral sympathetic nerve activity.

**Subjects** We examined 29 cases of type 2 diabetes that did not present autonomic dysfunctions (11 males and 8 females). The average age of the subjects was 64.9 years and the mean duration of diabetes was 13 years.

**Methods** MIBG uptake was quantified by calculation of the heart - mediastinum ratio (H/M ratio) that was calculated by average count per pixel in the regions of interest over heart and mediastinum on the planar anterior image of the chest. In addition, the washout rate (WR) was also calculated. SSR was performed followed by determination of amplitude and latency.

**Results** According to the results of 123I-MIBG myocardial scintigraphy, abnormalities in H/M ratio and WR were observed in 10 cases. Decreased amplitude was observed in 9 cases in SSR. H/M ratio and WR did not correlate with symptoms of diabetic peripheral neuropathy, and there was no correlation observed with the results of SSR as well.

**Discussion** 123I-MIBG myocardial scintigraphy, along with SSR, is a simple and objective evaluation method, and is considered to be a useful method for assessing early diabetic autonomic neuropathy.

#### P 2122

##### **Sympathetic skin response and foot ulceration in diabetes**

P. Kokotis<sup>1</sup>, A. Karanti<sup>3</sup>, N. Tentolouris<sup>2</sup>, P. Tsapogas<sup>2</sup>, N. Katsilambros<sup>2</sup>, U. Smith<sup>3</sup> and C. Karidakis<sup>1</sup>  
*<sup>1</sup>Neurological Department of Laiko Hospital, Athens, GREECE, <sup>2</sup>1<sup>st</sup> Department of Propaedeutic Medicine, Athens, University Medical School, Athens, GREECE, <sup>3</sup>Department of Internal Medicine, Sahlgrenska University Hospital, Gothenburg, SWEDEN*

**Background-Aims** This study examined the relationship between sympathetic skin response (SSR) as a reliable test of autonomic nervous system function and foot ulceration (FU) in diabetes.

**Materials and Methods** 64 patients with either type 1 or type 2 diabetes were studied. Diagnosis of peripheral sensory neuropathy (PN) was based on clinical symptoms, signs and vibration perception threshold. DS were divided in 3 groups: without

PN (DN- n=31), with PN (DN+ n=15), with neuropathic FU (DFU, n=18). SSR was performed at the dorsal aspect of the right foot after a surpamaximal electrical stimulation of the median nerve over the wrist of the right arm.

**Results** SSR was absent in all but 2 DS with DFU, in 6 out of 15 DS in the DN+ group and in 10 out of 31 DS in the DN-group. Statistical analysis using Fisher's exact test revealed a strong difference among the DS patients with or without FU ( $p < 0.0002$ ) while less strong but still significant among them with or without PN ( $p < 0.0118$ ), concerning the presence of the SSR response.

**Conclusions** There is an "all or none" correlation of SSR and FU and PN signs, as well, stronger for the first of them.

## P 2123

### Nerve conduction study in patients with diabetic neuropathy treated with alfa-lipoic acid

D. T. Bogdanova, I. Milanov

University Hospital of Neurology and Psychiatry "St. Naum", Sofia, BULGARIA

It has been reported that diabetic polyneuropathy treatment with alfa-lipoic acid may improve the subjective complains of limbs pain and paresthesias. However, it is controversial if the objective neurological symptoms of the polyneuropathy are improved. Although the electroneurography is a more precise method for diagnosis and follow up of the polyneuropathies, the published results regarding alfa-lipoic acid are also controversial.

The aim of this examination was to evaluate the efficiency of alfa-lipoic acid treatment of diabetic polyneuropathies using electroneurographic examination.

Thirty patients with clinical data for symmetric distal diabetic neuropathy were examined. The motor conduction velocities and M-wave amplitudes after fibular and tibial nerve electro stimulations were examined. The sensory nerve action potentials after sural and median nerve stimulations were also examined. The electroneurographic examination was performed before and after treatment. The alfa-lipoic acid was applied as a 600 mg daily intravenous infusion for 15 days, followed by 90 days oral intake of 600 mg daily.

The distal motor latencies of the tibial and fibular nerves were shortened significantly after the treatment, while no changes in M-wave amplitudes or motor conduction velocities were found. The distal latencies and the amplitudes of the sensory nerve action potentials were not significantly different after treatment.

In conclusion, our results revealed that high doses alfa-lipoic acid might improve the peripheral nerves function in patients with diabetic neuropathy. The small number of patients and the short treatment duration probably caused the controversial results.

## P 2124

### Screening dysarthria test for detection of dysarthria types in different neurological diseases.

B. Tomik<sup>1</sup>, I. Gatkowska<sup>2</sup>, M. Tutaj<sup>1</sup>, A. Pichor<sup>1</sup>, M. Bala-Słodowska<sup>1</sup>, M. Kusiak<sup>1</sup>, M. Rudzinska<sup>1</sup>, Z. Tarkowski<sup>3</sup>, A. Szczudlik<sup>1</sup>

<sup>1</sup>Department of Neurology CMUJ, Cracow, POLAND,

<sup>2</sup>Department of Psychology UJ, Cracow, POLAND, <sup>3</sup>Orator Foundation, Lublin, POLAND

**Background** The assessment of dysarthria types in the neurological clinical population is difficult. The current study proposes the simple screening test for detection and characterisation of dysarthria features in different neurological diseases.

**Material and methods** The study was performed in 78 dysarthric patients diagnosed with various neurological diseases in the Department of Neurology in Cracow during the year 2000–2001. The presence of dysarthria and its characteristic were assessed by means of a semi quantitative method, as is the "screening dysarthria test" (SDT) which is based on short-time assessment of dysarthria features as: respiratory control, articulation, phonation and prosody. The results were scored in a 4-points scale and compared with the results of Robertson's Dysarthria Profile Test (DPT) and clinical sings.

**Results** Mild shortening of respiratory cycle (92.9%), disturbances of phonation (92.9%), and well preserved prosody occurred in patients with spastic dysarthria (14 out of 78 patients). Pronounced shortening of respiratory cycle (70.6%), abnormalities of phonation (58.8%) were typical for patients with flaccid dysarthria (17/78). Dysprosody (86.7%) occurred predominantly in patients with ataxic dysarthria (15/78). The abnormalities of phonation (86.7%) and dysprosody (80%) were dominant in patients with hypokinetic dysarthria (15/78). The significant loss of respiratory control (100%) and dysprosody (75%) occurred in patients with hyperkinetic dysarthria (4/78) while phonation was merely preserved. All of dysarthria features measured were abnormal in patients with mixed dysarthria (13/78).

**Conclusion** Our results demonstrate the practical usefulness of SDT in detection and classification of dysarthria types that occur in different neurological diseases.

## P 2125

### Intramuscular olanzapine: efficacy and safety in acutely agitated patients with dementia

K. M. Meehan, H. Wang, S. R. David, J. R. Wright, B. Jones, C. M. Beasley Jr., P. D. Feldman, A. Breier

Lilly Research Laboratories, Indianapolis, IN, USA

**Objective** To investigate the efficacy and safety of rapid-acting intramuscular olanzapine in treatment of agitation in patients with dementia.

**Methods** Patients were randomised to receive up to 3 intramuscular injections within 24 hours: 2.5-mg olanzapine (Olz2.5, n=71), 5.0-mg olanzapine (Olz5.0, n=66), 1.0-mg lorazepam (Lzp, n=68), or placebo (n=67).

**Results** Two hours after injection1, olanzapine and lorazepam improved scores significantly more than placebo on the PANSS Excited Component subscale (PANSS-EC) and Agitation-Calmness Evaluation Scale (ACES). Olz5.0 and Lzp also improved scores more on the Cohen-Mansfield Agitation Inventory. At 24 hours, both Olz groups continued to show statistical superiority over placebo on the PANSS-EC, but Lzp did not. Simpson-Angus and MMSE scores did not change significantly from baseline. Sedation (ACES  $\geq 8$ ), adverse events, and laboratory analytes were not different from placebo for any treatment. QTc interval changes were not significantly different from placebo for any of the active treatments. No clinically and statistically significant changes were seen in any other vital signs, including orthostasis.

**Conclusion** These results suggest that rapid-acting intramuscular injection of olanzapine may provide substantial benefit in treating dementia-related agitation.

## References

Cohen-Mansfield J, Billig N, Lipson S, Rosenthal AS, Pawlson LG (1990). Medical correlates of agitation in nursing home residents. *Gerontology* 36:150–158  
 Deutsch LH, Rovner BW (1991). Agitation and other noncognitive abnormalities in Alzheimer's disease. *Psychiatr Clin North Am* 14:341–351

## P 2126

### Combined event-related fMRI and intracerebral ERP study of auditory oddball task

M. Brazdil<sup>1</sup>, M. Dobsik<sup>2,1</sup>, P. Daniel<sup>1</sup>, M. Pazourkova<sup>3</sup>, P. Krupa<sup>3</sup>, I. Rektor<sup>1</sup>

<sup>1</sup>Ist Dept. of Neurology, St. Anne University Hospital, Brno, CZECH REPUBLIC, <sup>2</sup>Faculty of Information Technology, University of Technology, Brno, CZECH REPUBLIC, <sup>3</sup>Dept. of Neuroimaging, St. Anne University Hospital, Brno, CZECH REPUBLIC

**Introduction** Event-related fMRI (efMRI) was repeatedly used to seek the neural sources of endogenous event-related potentials (ERP). Significant discrepancies between the efMRI data and the results of previously published intracranial ERP studies of oddball task were revealed.

**Methods** To evaluate the capacity of efMRI to define the sources of the P3 component of ERP within the human brain, both efMRI and intracerebral ERP recordings were performed in three patients with intractable epilepsy (two males and one female) during their preoperative invasive video-EEG monitoring. An identical auditory oddball task with frequent and target stimuli was completed in two sessions. A total of 237 intracerebral sites were electrophysiologically investigated by means of depth electrodes.

**Results** In accordance with the finding of multiple intracerebral generators of P3 potential, the target stimuli evoked MRI signal increase in multiple brain regions. However, regions with evident hemodynamic and electrophysiological responses overlapped only partially. A P3 generator was always found within a hemodynamic-active site, if this site was investigated by means of depth electrodes. On the other hand, unequivocal local sources of P3 potential were apparently also located outside the regions with a significant hemodynamic response (typically in mesiotemporal regions).

**Conclusion** Both methods should be viewed as mutually complementary in investigations of the spatial distribution of cortical and subcortical activation during oddball task.

MSMT CR Research Program no. 112801 supported the study.

## P 2127

### Effects of ecstasy in human EEG

M. Adamaszek

University Greifswald, Greifswald, GERMANY

**Aim** of the study was the detection of special EEG features in Ecstasy users, which might reflect the often-reported cognitive disturbances, essentially in mnemonic and attentional performance.

**Methods** 105 female and male polyvalent users with Ecstasy in former times as well as 41 matched persons with a comparable drug history and 11 drug abstinentes were included. Besides qualitative EEG measurements, power spectra had been formed and evaluated by SPSS package.

**Results** Ecstasy users with medium and high cumulated doses of Ecstasy revealed more often an increasing in Theta- (3.5–5.0; 5.0–7.5 Hz), lower Alpha- (7.5–9.0 Hz) and Beta-sub bands

(13.5–20.0–22.0 Hz), an slowing of dominant frequency, finally an increased power of slow frequencies in the early situation (first 2 minutes) of EEG-derivation. However, female Ecstasy users showed more pronounced dose-depending effects. For covariate calculations, the relationship remained significant after controlling for covariant medication.

**Conclusion** Because of the neurotoxic effects of Ecstasy and its substantial compounds like MDMA or MDE predominantly for 5-HT-specific neurons the results with significant increases even in the 5- and 20-Hz-frequencies reflect dysbalances of serotonergic projections within the subcortical vigilance-regulating systems of the human CNS, indicating neuropathophysiological basic mechanisms of the frequently observed mnemonic and attentional deficiencies in Ecstasy users.

## P 2128

### Impact on cortical excitability during unilateral electroconvulsive therapy: a pilot study

A. Conca<sup>1</sup>, S. Koppi<sup>2</sup>, P. Wartberger<sup>2</sup>

<sup>1</sup>Department of Psychiatry, LKH Rankweil, Rankweil, AUSTRIA, <sup>2</sup>Department of Neurology, LKH Rankweil, Rankweil, AUSTRIA

**Introduction** Paired pulse transcranial magnetic stimulation (ppTMS) is a non-invasive, painless and safe diagnostic method to analyse the phenomena of intracortical, transsynaptic inhibition and facilitation. The aim of this pilot study was to investigate the effects of the electroconvulsive therapy (ECT) on motor excitability as measured by ppTMS.

**Methods** In three, drug-free, right-handed remitted depressive patients undergoing maintenance unilateral ECT (over the right hemisphere) ppTMS was performed before and after the stimulation session.

**Results and conclusion** The results revealed predominantly left-sided marked changes of the inhibition and facilitation intracortical activities in two patients after the ECT; thereby a significant increased excitability and important decreased intracortical inhibition could be observed indicating a contra lateral disinhibition effect of ECT. This mechanism of action could be analysed only in the two patients revealing a good clinical outcome; thus, marked changes of cortical excitability may be correlate to the efficacy of ECT.

## P 2129

### Treatment for dystonia of the autonomic nervous system

Z. A. Mirzadjaniva<sup>1</sup>, H. Mahkamova<sup>2</sup>

<sup>1</sup>Republican Scientific Centre of Neurosurgery, Tashkent, UZBEKISTAN, <sup>2</sup>Department of Neurological Disorders, Tashkent, UZBEKISTAN

The InfraR method has been used to treat dystonia of the autonomic nervous system (DANS). All the subjects were divided into 3 groups: 1) healthy volunteers, 2) people suffering from DANS (caused by neuroses and acute and chronic stress), and 3) people with DANS who were not to be given treatment by the InfraR method. The DANS patients had both permanent and paroxysmal manifestations as panic attacks. To assess the effectiveness of the therapy we monitored: the functional status of the ANS using the Guillaume–Wein table and the Aschner-Dagnini and postural tests, and the psychoemotional state of the subjects using the Spielberger anxiety inventory.

Analysis of the data for the group 2 patients revealed that the use of the InfraR method normalizes the functional status of the ANS. An investigation into the autonomic support of activity prior to treatment detected a rise in heart rate; a postural test did

not bring about a significant decrease in heart rate and the heart rate did not return to the initial values. On day 10 of treatment an examination of heart rate and blood pressure in this group revealed normal responses. The Spielberger anxiety inventory showed a perceptible diminution in the anxiety levels.

In-group 3 the treatment gave rise to little change in the functional status of the ANS. Thus, the treatment by the InfraR method has a relaxing effect on the psycho autonomic system and can be used as an adequate nonpharmaceutical treatment for DANS.

P 2130

**Supine-standing-supine test in diabetic autonomic neuropathy diagnostics: a contribution to the assessment of vagal activity with the use of short-term spectral analysis of heart rate variability**

J. Opavsky, J. Salinger

*Faculty of Physical Culture, Palacky University, Olomouc, CZECH REPUBLIC*

**Introduction** The purpose of this study was to prepare a simple procedure for diagnosing autonomic neuropathy (AN) in routine clinical practice. It was based on shifts in sympatho-vagal balance induced by body position changes during the carrying out of the supine1-standing-supine2 test.

**Methods** The study was conducted on 39 Type 1 and 13 Type 2 diabetic patients (DP) (mean age of 37.8 and 55.0 years, respectively). The autonomic activity was assessed using spectral analysis of heart rate variability. In short-term recordings, the values of the spectral power (SP) of the low-frequency component (LF, 0.05–0.15 Hz), high-frequency component (HF, 0.15–0.50 Hz) and total spectral power (LF+HF) in all body positions – i.e. in supine1-standing-supine2 test – were registered. The vagal activity (SP of HF component) was compared in supine1 and supine2 positions.

**Results** The mean values of SP of HF component were found in subjects without peripheral and AN (n=6) in supine1 and supine2 positions 1426.4 and 2164.9 ms<sup>2</sup>, respectively. The mean values of SP of HF component in DP with early AN (n=10) were in the same positions 91.4 and 292.8 ms<sup>2</sup>. The DP with definite parasympathetic AN (n=10) expressed the corresponding values of 80.2 and 146.9 ms<sup>2</sup>.

**Conclusion** In all three subgroups of DP in the repeated supine position (supine2), the higher values of SP of HF component were registered, reflecting the overshoot of vagal activity after orthostatic load in the preceding standing position. Thus, in the supine2 position, a reserve of full vagal activity could be revealed.

P 2131

**Assessment of dysautonomia in various myopathies**

M. Nojszewska, A. Kostera-Pruszczyk,

B. Zakrzewska-Pniewska

*Medical University of Warsaw, Warsaw, POLAND*

Dysautonomia is rarely of clinical significance in myopathies excepting the Emery-Dreyfuss progressive muscular dystrophy. We used two non-invasive electrophysiological tests: the R-R interval variation (RRIV) and sympathetic skin response (SSR) to verify their usefulness in the assessment of dysautonomia in myopathies of different aetiology. RRIV and SSR were studied in a group of 25 myopathic patients (13 children and 12 adults) with Duchenne, Becker and Emery-Dreyfuss progressive muscular dystrophies, myotonia congenita, paramyotonia congenita, myotonic dystrophy, mitochondrial myopathy and polymyositis.

Clinical symptoms of dysautonomia were evaluated using Autonomic Symptoms Questionnaire (Low). Such symptoms were found in 13 patients whereas the RRIV and/or SSR were abnormal in 6. The RRIV abnormalities (decreased R-R variability) were observed in 3 adult patients; the SSR abnormalities (delay in latency) in 1 child and 5 adults. The clinical symptoms of dysautonomia as well as the RRIV and SSR abnormalities were less frequent and less severe in children with myopathies if compared with adult patients. Our study has revealed that RRIV and SSR were rarely abnormal in myopathies, especially in children and that those methods although non-invasive are not very sensitive and useful for the detection of discrete autonomic imbalance in patients with myopathies.

P 2132

**Autonomic disorders are associated more often with an akinetic-rigid component in Parkinson's disease**

D. Tiple<sup>1</sup>, I. Moldovanu<sup>2</sup>, V. Vovc<sup>2</sup>, S. Odobescu<sup>2</sup>

*<sup>1</sup>Scientific and Practical Centre of Neurology and Neurosurgery, Chisinau, REPUBLIC OF MOLDOVA, <sup>2</sup>SPCNN, Chisinau, REPUBLIC OF MOLDOVA*

**Introduction** Autonomic disorders are common complications in Parkinson's disease (PD). For most patients dysautonomias are overshadowed by the more prominent motor dysfunction. However, a significant minority of PD patients experiences severe and disabling autonomic impairment. The pattern of autonomic disorders was studied depending on the PD form.

**Methods** 32 patients were subjected to this study, with mean age 56 (ranging 36–75), split into three groups depending on the PD form, and 14 healthy people (control group). The motility was tested by UPDRS. Cardiovascular tests were used as autonomic tests (deep slow breathing test, 30/15 test, Valsava test, orthostatic test, isometric test).

**Results** 8 patients with akinetic-rigid form were included into the first group, 11 with tremor into the second group, and 13 with a mixed form - into the third group. Mean age by group – 52.3, 61.4 and 54.3 years respectively. In the three groups, total UPDRS score was 62, 48 and 89 points respectively. Duration of PD course in three groups was 4.1, 6.3 and 6.1 years. Clinical autonomic disorders (constipation, sexual problems) – 6 (75%), 2 (18.1%), and 8 (61.5%) respectively. Abnormal autonomic values were registered in 6 patients (75%), 3 (27.2%), and 9 (69.2%) in the three groups respectively.

**Conclusion** Autonomic disorders are more often associated with akinetic-rigid PD form and are not related to the patient's age, length of disease or use of dopaminergic drugs. The cause is abstruse and possibly depends on the selectively impaired structures in one or another form of the disease.

P 2133

**Physiological asymmetry of peripheral vasomotor reaction: telethermographic study with fist cricoactivation**

D. Alvir, D. Petracic, N. Zurak, V. Matijevic, S. Supe  
*University Hospital Zagreb, Zagreb, CROATIA*

The **aim** of the study is to find out if the asymmetry of vasomotor reaction, following fist cricoactivation, was related to the hand preference of the examinee.

**Methods** 90 healthy examinees 20–50 years old, 47 females, 43 males with right hand preference, according to The Annet Handedness Questionnaire, have been screened. Telethermographic pictures of hand dorsum were taken with computerized AGA Thermovision 782 infrared camera, prior and upon cricoactivation /12 times – sampling 1 minute/. Cricactivation was

obtained by 1 minute emerging randomly selected hand in 5 litre of cooled water  $\pm 4$  C°. The same procedure was repeated 4 hours later with another hand under equal exterior conditions. Hand dorsum temperature taken 1 minute upon reactivation and time required for restitution back to the pre-activation temperature, were statistically analysed by Wilcoxon signed ranks test.

**Results** There was stronger vasoconstriction on dominant right fist /median 23.8 C° min. 13.3, max. 33.1 vs. median 24.9 C°, min. 15.3, max. 30.1;  $p < 0.01$ / 60 examinees have reached hand dorsum temperature restitution in 12 minutes. There was faster restitution of dominant right fist /median 8 minutes, min. 5, max. 12 vs. median 9.5 minutes, min. 8, max. 11;  $p < 0.001$ .

**Conclusion** Presented results show that the reaction of autonomic nervous system, as main vasomotor reaction control system, is more efficient on the side of the dominant hand. Further investigation is needed for confirmation of this physiological method as possible hand preference screening procedure.

#### P 2134

##### Evaluation of the cardiovascular autonomic functions in diabetic patients

I. Velcheva, P. Damianov, E. Titianova  
Medical University, Sofia, BULGARIA

Diabetes mellitus is known to be associated with peripheral nerve lesions where sensory and motor disturbances are the most frequent and the autonomic disturbances are more rare.

The aim of our study was to evaluate the changes in some cardiovascular autonomic tests in 40 diabetic patients aged 32 to 57 years. Twenty of the patients had non-insulin dependent diabetes mellitus (NIDDM) and another 20-insulin dependent diabetes mellitus (IDDM); all of them had diabetic polyneuropathy with sensory or motor signs and conduction disturbances.

The RR variations during deep breathing, the Valsalva manoeuvre, tilt and active standing were recorded and the heart rate response to deep breathing (HRdb), the Valsalva ratio (VR) and the 30:15 ratio were calculated. Also, the beat-to-beat blood pressure response to standing was measured with a non-invasive instrument (Colin 7000, Medical Instruments Group, USA). The data obtained were compared with a control group of 40 healthy subjects in the same age group.

Our results reveal abnormal cardiovascular responses with significant decrease of the HRdb response, the VR and of the 30:15 ratio in the patients in comparison to the controls. Orthostatic hypotension was found in 25%. The abnormalities were asymptomatic in 15% of the patients. They were more pronounced in the subgroup with NIDDM. Their frequency correlated with longer duration of the diabetic disease.

Conclusion is drawn for the clinical significance of the autonomic testing of the diabetic patients.

#### P 2135

##### Effect of hyperventilation on visual evoked potential

M. Moghaddasi<sup>1</sup>, B. Zamani<sup>1</sup>, A. Freydoonjad<sup>2</sup>,  
M. Mehrpoor<sup>1</sup>

<sup>1</sup>Rasool Akram Hospital, Iran University of Medical Sciences, Tehran, ISLAMIC REPUBLIC OF IRAN, <sup>2</sup>Ministry of Petroleum Main Hospital, Tehran, ISLAMIC REPUBLIC OF IRAN

We compared the effect of hyperventilation on pattern-shift visual evoked potential in 32 patients with definite multiple sclerosis and 30 normal subjects. There was a significant reduc-

tion in p100 latency in patients with multiple sclerosis and optic neuritis compared with normal subjects. It seems that there is an improved impulse transmission in demyelinated fibers that may be due to alkalosis and changes in ionised calcium level due to hyperventilation.

#### P 2136

##### Changes in motor and sensory nerve conduction parameters with temperature in normal subjects and patients with multiple sclerosis

E. Hidasi<sup>1</sup>, D. Bereczki<sup>1</sup>, T. Csépanyi<sup>1</sup>, F. Mechler<sup>1</sup>,  
P. Diószeghy<sup>2</sup>

<sup>1</sup>University of Debrecen, Debrecen, HUNGARY, <sup>2</sup>Jósa András Hospital, Nyíregyháza, HUNGARY

The effects of temperature on motor and sensory nerve conduction parameters were studied in 13 patients with multiple sclerosis and in 13 age- and gender-matched controls.

The motor and sensory conduction velocities, the distal and proximal latencies, the amplitude, duration and area of the compound muscle action and sensory nerve potentials of the median nerve were correlated with skin temperature gradually changed from 20 to 40°C. The differences in these parameters between the control and MS groups were also evaluated. Multiple regression statistical analysis was performed.

The latency, amplitude, duration and area of the motor and sensory potentials were increased, the conduction velocity decreased in lower temperatures. We found significant differences between the two groups in the values of the distal and proximal motor latencies and in the latency, amplitude and area of the sensory potentials. The distal ( $p = 0.00021$ ) and proximal ( $p = 0.00016$ ) motor and sensory latencies ( $p = 0.0097$ ) were significantly longer in the MS patients, than in the controls, and the increase of the latencies were most prominent in the lower temperatures (20–25°C) compared with controls. The sensory amplitude ( $p = 0.0047$ ) and area ( $p = 0.0067$ ) were significantly less in the MS patients, but these differences didn't change with the alteration of temperature.

The elevation of temperature may produce clinical worsening of multiple sclerosis. It is very interesting, that we found a more prominent increase of motor latencies in MS patients in lower temperatures, since it reflects more severe dysfunction of neuromuscular transmission in colder circumstances.

#### P 2137

##### Brain bioelectric activity in Belarussian children irradiated in utero as a result of Chernobyl accident

S. Igumnov, L. Shalkevich

Belarussian Medical Academy of Postgraduate Training,  
Minsk, BELARUS

**Objective** The study examined the formation of bioelectric activity (BEA) of the brain in 250 children at 10–12 years of age from regions highly contaminated by Chernobyl fallout, who were irradiated in the prenatal period at the time of the Chernobyl accident in 1986. These children were compared to a control group of 250 children of the same age from non-contaminated areas of Belarus.

**Methods** The examination included visual and computerized analysis of electroencephalography (EEG) as well as psycho-neurological examination and assessment of intellectual level.

**Results** In both groups of children at the age of 10–12 the dominants were the variants of age norms (54.4% vs. 52.8%;  $p = 0.719$ ) and synchronized (borderline) EEG (28.8% vs. 34.4%;  $p = 0.178$ ). Quite noticeable was the relevant frequency

of the slow type of EEG (11.6% vs. 7.2%;  $p=0.092$ ) as well as paroxysmal activity (5.2% vs. 6.0%;  $p=0.698$ ) in both groups. The correlation analysis showed that the intellectual level of children (IQ) estimated by Wechsler Intelligence Scale (WISC-III) was in direct proportion to spectral power of  $\alpha$ -dipason in frontal lobes of the brain ( $r=0.38$  in both groups).

**Conclusions** The revealed changes of BEA of the brain show distinct age dependency. Their frequency in children exposed to antenatal irradiation does not have any relevant differences from that in the control group.

P 2138

**Normative values and intra-individual variability of thermal threshold testing**

E. Moravcova, J. Bednarik

*Department of Neurology, University Hospital, Brno, CZECH REPUBLIC*

**Introduction** The thermal threshold testing method (TTT) is a quantitative sensory test based on the psycho physiological principles of thermal threshold and the relation between the supra-limbar stimulus and its response. There is a paucity of data referring to the influence of physiological variables upon the normal limits and to the intra-individual variability of this psycho physiological test. The objective of this study was to establish normative values and to assess trial-to-trial variability of threshold values.

**Methods** A thermal threshold for cold and warm sensation was established in a group of 50 healthy volunteers in two locations (the thenar of the hand and the dorsum of the foot) using a Medoc Thermal Sensory Analyser software. All individuals were examined with 3 different algorithms: two reaction-time inclusive methods (RTI-Limits I and II) and one reaction time-exclusive method (RTE-random variant of Levels). All tests were repeated for 30 individuals within 1 week to assess the intra-individual variability.

**Results** The values for the cold threshold decreased significantly and those of warm threshold increased with age, in men, and when using the RTI methods. Trial-to-trial variability of threshold values expressed as the mean day-to-day variation coefficient varied between 19 and 49% independent of algorithm type employed, of the tested region, age or sex.

**Conclusions** Normal limits for different age and sex groups are needed. The intra-individual variability of the threshold values is acceptable with respect to the psychophysical character of the test and comparable with other quantitative sensory tests.

Supported by IGF FN Brno grant No15/2000.

P 2139

**Suprasegmental muscular pareses in patients with lumbar spine discal hernias**

T. Styczynski, R. Gasik

*Institute of Rheumatology, Warsaw, POLAND*

**Introduction** The discal hernias arising from the given spinal segment cause destruction of the nerve roots and pareses of the muscles innervated by segment where "discal-root conflict" occurs. But question is, if it is always true?

**Methods** In 41 patients, in whom the MRI studies revealed discal hernias of L4/L5 and L5/S1 with the compression of the L5 and lower located nerve roots, the isometric tests of the thigh quadriceps strength in both legs (innervated by the L2 to L4 nerve roots). In 14 patients, additional bilateral electromyographic tests of these muscles were carried out.

**Results** The dynamometric tests of the knee extensor muscles carried out in standard conditions with identical force arm, revealed, at the side of the root syndrome the average force of 104.4 N, and at the contra-lateral side on average 156.8 N. The average strength deficit at the side of the root syndrome of 52.4 N corresponds to 33.3% deficit in comparison to the contra-lateral side.

The EMG studies of the quadriceps muscle provided normal results in 5 (35.7%) patients and in 9 (64.3%) there were signs of neurogenic muscle damage found.

**Conclusion** The results of the studies indicate, that in the patients with discal hernias there are pareses found not only in the segmental muscles of the "discal-root conflict" but also in the muscle innervated by the nerve roots located above it. Regardless of the mechanism leading to these pareses, (vascular lesions?) their presence has to be considered in planned rehabilitation and management.

P 2140

**Subclinical nerve conduction abnormalities in children with diabetes type I**

D. Chkhartishvili, N. Khachapuridze

*Tbilisi State Medical University, Tbilisi, GEORGIA*

**Introduction** Diabetic peripheral polyneuropathy, which is often seen in adult patients with diabetes type II, is characterized by distal symmetric sensorimotor disturbances. Focal nerve and proximal motor (amyotrophy) impairments are not as common though and have a putative inflammatory, vasculitic or autoimmune origin. Autonomic nervous system disorders are also frequently seen in adult diabetics.

**Methods** We performed nerve conduction studies (NCS) in 52 children 6–16 year-old (25 males) with diabetes type I, without any clinical sign of neuropathy. NCS included testing of median, ulnar, peroneal and tibial motor nerve conduction velocities (MNCVs) and M-response amplitudes bilaterally by medicor type MG440 electromyograph. A control group included 20 healthy children 6–16 yrs. old.

**Results** In a first group of 30 children (6–10 y) with disease duration <5 y. whose metabolic control was clinically well compensated, we revealed near normal NCS features comparable with those of age-matched controls. ( $P<0.001$ ). In a second group of 22 children (11–16 y) with disease duration >5 y, and poor metabolic control, we found abnormally slow MNCVs and considerably prolonged distal latencies, with significantly decreased M-response amplitudes in all above nerves. All abnormalities were symmetric ( $P<0.001$ ). Autonomic nervous system tests did not reveal any disturbances. Children remained clinically asymptomatic for a <2.5 y follow up.

**Conclusion** In children with poorly compensated diabetes type I NCS may reveal subclinical abnormalities that are suggestive of symmetrical distal polyneuropathy.

P 2141

**Effect of chronic hypoxia on the nervous system: visual and auditory brainstem evoked potentials in patients with chronic obstructive pulmonary disease**

S. M. A. Said<sup>1</sup>, A. Enan<sup>2</sup>, E. Saleh<sup>1</sup>

<sup>1</sup>Alexandria University, Alexandria, EGYPT, <sup>2</sup>Zagazig University, Banha, EGYPT

**Objectives** We aimed at studying the effect of chronic hypoxia associated with chronic obstructive pulmonary disease (COPD) on the nervous system.

**Background** Several recent neurophysiological studies had shown the deleterious effect of chronic hypoxia associated with COPD on the peripheral as well as the central nervous system. However, no correlation was found between hypoxia and any of the neurophysiological abnormalities.

**Design and methods** Participants consisted of 22 patients with moderate-severe COPD male patients aged 60–72 years (mean  $\pm$  s.d. =  $67 \pm 4.42$ ). Twenty age-matched non-smoking healthy male controls were also recruited. We performed pulmonary function tests, arterial blood gas analysis, audiogram, auditory brainstem evoked responses (ABR) and visual evoked potentials (VEP) for all patients and controls.

**Results** ABR were abnormal in 18 (81.82%) of the 22 COPD patients. Most prominent ABR abnormalities were prolonged wave I peak latency ( $2.5 \pm 0.54$  msec), wave V peak latency ( $7.54 \pm 1.94$  msec) and I–V interpeak latency ( $5.05 \pm 1.49$  msec). There were significant negative correlations between PaO<sub>2</sub> and wave I peak latency ( $p < 0.05$ ). There were also significant positive correlations between PaCO<sub>2</sub> and wave V peak latency, I–V and III–V interpeak latencies ( $P < 0.01$ ). Lastly, there was a significant correlation between the Forced Expiratory Flow 25–75% and all ABR abnormalities. VEP study showed that the P100 was mildly but insignificantly delayed in COPD patients.

**Conclusions** The degree of affection of the nervous system in COPD patients is significantly correlated with the stage of the disease and the degree of hypoxia and hypercapnea.

#### P 2142

##### **Contributions of microneurography to the study of the pathophysiology of neuropathic pain**

J. Serra

*Clinica Sagrada Familia, Barcelona, SPAIN*

Patients with peripheral neuropathy commonly express positive sensory symptoms, such as tactile paresthesias, dysesthesias and pains. As opposed to negative sensory phenomena whose electrophysiological correlate can be readily measured through conventional laboratory methods, the study of positive sensory phenomena relies largely on quantitative psychophysical tests. In animals, possible electrophysiological correlates of positive sensory phenomena have been documented in traumatic neuromas and in demyelinated nerve fibers. In experimental human volunteers, ectopic nerve impulses generated in single myelinated sensory fibers have been correlated with post-ischemic and post-tetanic paresthesias. In patients, abnormal nerve impulse activity in afferent fibers has occasionally been recorded in polyneuropathy, amputation neuroma, and Spurling and Tinel's signs. In all cases, such activity was either spontaneous or elicited by mechanical stimuli applied at injured midaxon level. In addition to spontaneous ectopic activity, generation of abnormal nerve impulses in hyperexcitable myelinated fibers in patients with peripheral neuropathy and positive sensory symptoms has also been recorded.

Recent microneurographic techniques permit recording from individual unmyelinated C fibers and allow their segregation into different functional classes having discrete electrophysiological properties of their membranes. Particularly important for the study of physiological and neuropathic pain is the recording from mechano-sensitive as well as mechano-insensitive, or silent, nociceptors. Recent findings will be presented and their pathophysiological implications for the study of neuropathic pain will be discussed.

#### P 2143

##### **Pain related laser evoked potentials in multiple sclerosis patients**

H. Acar<sup>1</sup>, K. Durak<sup>2</sup>, F. Aysal<sup>1</sup>, S. Karamurzel<sup>3</sup>, I. Kara<sup>4</sup>, A. Nurten<sup>4</sup>, M. Ozturk<sup>1</sup>, S. Baybas<sup>1</sup>, A. C. N. Chen<sup>2</sup>, L. Arendt-Nielsen<sup>5</sup>

<sup>1</sup>Bakirkoy Ruh ve Sinir Hastaliklari Hastanesi 2 Noroloji Klinigi, Bakirkoy Istanbul, TURKEY, <sup>2</sup>SSK Vakif Gureba Egitim Hastanesi Noroloji Klinigi, Istanbul, TURKEY, <sup>3</sup>Istanbul Universitesi Istanbul Tip Fakultesi Fizyoloji AD, Istanbul, TURKEY, <sup>4</sup>Istanbul Universitesi Deneysel Tip Arastirma Enstitüsü Sinirbilim AD, Istanbul, TURKEY, <sup>5</sup>University of Aalborg Centre For Sensory-Motor Interaction, Aalborg, DENMARK

Pain Related Laser Evoked Potentials are being used to examine the thin nerve fibers carrying the pain and temperature sensation and the processing of this data at the Central Nervous System (CNS). Multiple Sclerosis (MS) is a disease mainly affecting the CNS. To investigate MS, the evoked potentials are widely used for years in order to determine the extension of the disease in CNS. Visual, sensorial and brain stem auditory evoked potentials are well known procedures. With these methods, the myelinated nerve fibers of the sensory system can be examined but the pain and temperature carrying system cannot.

In this study, 8 MS patients with spinal involvement and 9 healthy subjects were stimulated with diode laser on 8 different body area covered with hairy skin. The data were recorded from the scalp with 30 electrodes using Neuroscan. The amplitude brain maps were examined to understand the processing of pain in CNS and compared with the normal subjects. In some of the patients, there was no response or the latencies and the amplitudes were different from the control group and these were correlated with the lesions. In some other patients, examining the brain maps, the spatiotemporal development of the potentials in the CNS was found to be different and these were also thought to be correlated with the lesion distribution.

As a conclusion Laser Evoked Potentials using diode laser and brain mapping technique, are useful in determining the involvement of CNS and understanding the plastic changes in pain processing.

#### P 2144

##### **Motor Evoked Potentials (MEP) for intraoperative, sensorimotor differentiation of nerve fascicles without histochemical laboratory: an experimental study on sheep**

E. Turkof<sup>1</sup>, M. Reichel<sup>2</sup>, W. Mayr<sup>2</sup>, E. Unger<sup>2</sup>, M. Frey<sup>1</sup>

<sup>1</sup>Department of Plastic and Reconstructive Surgery, University of Vienna, Vienna, AUSTRIA, <sup>2</sup>Department of Biomedical Engineering and Physics, University of Vienna, Vienna, AUSTRIA

**Ratio and aim** Since microsurgery has been introduced in nerve reconstruction, surgeons have been seeking for a simple method to differentiate sensory from motor fibres in order to place nerve grafts on (functionally) corresponding fascicles on the cross-section of the nerve. Staining methods are time consuming and require an experienced laboratory staff. Since MEP is said to exclusively stimulate the motor cortex, we hypothesized that an evoked motor nerve action potential would exclusively follow the motor fascicles on the way to its target muscle.



Assumed that there is no functional exchange between sensory and motor fascicles along a peripheral nerve, the recording of nerve action potential from a nerve's surface subsequent to an MEP-stimulus would identify the very nerve to be a motor nerve. The goal of this study was to verify this hypothesis.

**Methods** 10 sheep were enrolled in this experimental study. Animal's ulnar nerves were exposed and the most distal bifurcation of the nerve into the last sensory and motor branch dissected. Electrical stimulation of both branches confirmed their functional identity, as did the post-mortem cross-sectional staining. Next MEP was performed and the evoked motor nerve action potentials simultaneously recorded from both remnant branches. (2 channel preamplifier, Viking-Quest-portable electromyograph).

**Results** In all ten sheep, recordings occurred on the motor branches alone.

**Conclusion** Intraoperative MEP is an effective tool to differentiate between motor and sensory nerve branches. Further studies are necessary to enable this technique on intact nerve trunks in order reach clinical applicability, where separation of fascicles is impossible.

P 2145

**Intraoperative electroneuro-diagnostics with transcutaneous, electrical stimulation of the spinal roots in routine peripheral nerve surgery: results of a prospective study on 110 nerves**

E. Turkof<sup>1</sup>, M. Reichel<sup>2</sup>, W. Mayr<sup>2</sup>, E. Unger<sup>2</sup>, M. Frey<sup>1</sup>  
<sup>1</sup>Department of Plastic and Reconstructive Surgery, University of Vienna, Vienna, AUSTRIA, <sup>2</sup>Department of Biomedical Engineering and Physics, University of Vienna, Vienna, AUSTRIA

**Ratio and aim** Frequently, plastic surgeons have to face controversial NCV-studies, and often-exposed nerves do not show any pathological aspect. The goal of this prospective study was to investigate the possible benefit of the routine application of intraoperative electroneuro-diagnostics (IOE) in peripheral nerve surgery. Specifically, how frequently the intraoperative determination of the site and proximal extent of nerve lesions provides information leading to a change of the initial surgical concept?

**Patient and methods** 110 peripheral nerves from 95 patients suffering from various types of lesions have been measured during surgery. Following exposure, the surgical concept was decided without implementing IOE. Subsequently, patients were fully relaxed and spinal roots of the damaged nerves transcutaneously stimulated with surface electrodes placed paravertebrally on the ipsilateral side over the respective nerve segments (Digitimer D185, monophasic square wave pulse, 50 µsec duration, 300–1000 volts, according to the security standards of the EC-maximum load/stimulus: 330 millijoule). Nerve compound action potentials were recorded with a bipolar electrode moved proximally and distally along the surface of the nerve.

**Results** In 21 cases (19%) the recording lead to important changes of the initial surgical concept or provided crucial information otherwise not obtained, in 8 cases the measurements confirmed the solely clinically based surgical indication despite controversial preoperative NCV studies.

**Conclusion** IOE is a valid, simple, reliable and effective tool to detect the exact site and proximal extent of nerve lesions. The routine implementation of IOE can be recommended.

P 2146

**Biphasic stimulation: a new technique to reduce the stimulus artefact during motor evoked potentials in brachial plexus surgery**

E. Turkof<sup>1</sup>, M. Reichel<sup>2</sup>, W. Mayr<sup>2</sup>, E. Unger<sup>2</sup>, H. Millesi<sup>3</sup>  
<sup>1</sup>Department of Plastic and Reconstructive Surgery, University of Vienna, Vienna, AUSTRIA, <sup>2</sup>Department of Biomedical Engineering and Physics, University of Vienna, Vienna, AUSTRIA, <sup>3</sup>Vienna Private Hospital, Vienna, AUSTRIA

**Ratio and aim** Since 1990, Motor Evoked Potentials (MEP) have been implemented during brachial plexus surgery to detect intradural avulsions of anterior motor roots. However, difficulties to record the evoked potential from the exposed spinal nerves hindered the wide application of the method. The reason for this problem are the commonly available electrical stimulators which provide a *monophasic* electrical pulse: every rising edge of a pulse leads to a charging current, and every falling edge to a discharging current: both spread within the tissue as a resulting current after the second (falling) edge. This spreading can last few milliseconds, and if the expected recording appears within this time period, the signal to be recorded is out of measuring. The aim of this study was to find a way to stimulate the central cortex (MEP) with sufficiently low artefact to enable reliable recordings of short latencies.

**Material and methods** We developed an electronic device able to deliver a biphasic stimulation pulse, which consists of a first rising, a second falling and a third (again) rising edge. This approach should reduce the amount of spreading current by adding another, but reversibly charged current after the end of the falling edge of the first pulse. This method has been applied to five healthy spinal nerves during brachial plexus surgery.

**Results and conclusion** In all cases, the length of the trigger artefact could be kept around 1 ms. Measurements with monophasic stimulation technique showed trigger artefacts with distinctly higher amplitudes and longer durations. The biphasic technique enables recordings that are more reliable.

P 2147

**Comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with dysphagia in a neurological department**

E. Ehler<sup>1</sup>, P. Geier<sup>1</sup>, P. Vyhnalek<sup>2</sup>  
<sup>1</sup>Dept. Neurology, Hospital Pardubice, CZECH REPUBLIC, <sup>2</sup>Dept. Internal Medicine, Hospital Pardubice, CZECH REPUBLIC

**Objectives** The use of percutaneous endoscopic gastrostomy [PEG] tube feeding is now more frequent and the indication is not restricted only to patients with more than 6 weeks lasting dysphagia. The aim of the retrospective study was to compare the range of indications for PEG or nasogastric tube [NGT] insertion, to state the complications, to evaluate the advantages and disadvantages of both enteral feeding methods.

**Patients and methods** Group A: 62 patients with PEG tube hospitalised in neurological department [ward and ICU] from 1. 7. 1997 till 31. 12. 2001, average age 72.4+/-14.3 years, 31 women and 31 men. PEG was inserted in 56 patients with acute neurological disorders with an interval of 24.8+/-15.6 days since the event. Chronic progressive neurological diseases were in 6 patients.

Group B: 72 patients with NGT were hospitalised during one year [2001] at neurological ICU, average age 75.6+/-11.1 years. 37 women and 35 men.

**Results** NGT was inserted more frequently in patients with bad life prognosis, in more patients with cerebral haemorrhages, brain tumours and epileptic states than was PEG. The complication rate was nearly the same in both groups [25.8% vers. 25%]. Special indications for an earlier PEG tube insertion: patients with tracheostomy, confused and non-compliant patients with NGT irritation, aphasic patients with a need of logopaedic therapy.

**Conclusion** PEG is a safe method of tube feeding and after nearly 5-years experience; we have found the earlier and specific indication in patients with acute neurological disorders.

P 2148

#### Evaluation of compound muscle action potential shape

V. Khodulev<sup>1</sup>, N. Nechipurenko<sup>1</sup>, V. Ponomarev<sup>2</sup>

<sup>1</sup>Research Institute of Neurology, Neurosurgery and Physiotherapy, Minsk, BELARUS, <sup>2</sup>Hospital # 5, Minsk, BELARUS

## Headache and pain 1

P 2149

#### Evidence for cortical functional changes in patients with migraine and white matter abnormalities on conventional and diffusion tensor MRI

M. Filippi, M. A. Rocca, B. Colombo, E. Pagani, A. Falini, G. Scotti, G. Comi

*Ospedale San Raffaele, Milan, ITALY*

**Introduction** We used functional magnetic resonance imaging (fMRI) to investigate the pattern of cortical activations following a simple motor task in patients with migraine and white matter (WM) abnormalities on conventional MRI scans of the brain. We also investigated whether the extent of brain activations was correlated with WM structural pathology measured using diffusion tensor (DT) MRI.

**Method** From 15 right-handed patients with migraine and 15 sex- and age-matched, right-handed healthy volunteers, we obtained: a) fMRI (repetitive flexion-extension of the last four fingers of the right hand); b) dual-echo turbo spin echo scans, and c) pulsed-gradient spin-echo echo-planar sequence to calculate DT-MRI maps. fMRI analysis was performed using statistical parametric mapping (SPM99) and cluster detection. Mean diffusivity (MD) histograms of the normal-appearing WM (NAWM) were also produced.

**Results** Compared to healthy volunteers, migraine patients had a larger relative activation of the contralateral primary sensorimotor cortex ( $p=0.01$ ), and a rostral displacement of the supplementary motor area (SMA) ( $p=0.03$ ). The shapes of the curves reflecting the time course for fMRI signal intensity changes were similar between migraine patients and controls for all the cortical areas we studied. Compared to healthy subjects, migraine patients had significantly lower MD histogram peak height of the NAWM histogram ( $p=0.02$ ), which was found to be correlated with the extent of displacement of the SMA ( $r=-0.80$ ,  $p<0.001$ ).

**Conclusion** This study suggests that functional cortical changes occur in patients with migraine and brain MRI abnormalities and that they might be secondary to the extent of subcortical structural damage.

P 2150

#### Colour visual evoked potentials in migraine

M. De Marinis, M. Oratino, L. Natale, N. Accornero

*Dept. of Neurological Sciences – “La Sapienza University”, Rome, ITALY*

**Introduction** The occipital cortex is thought to be involved in migraine. Increase in VEPs amplitude and decrease in habituation to repetitive visual stimulations have been considered signs of visual cortex hyperactivity in this disease. However, there is also evidence for hypoexcitability of visual cortex in headache-free migraine patients studied with transcranial magnetic stimulation.

**Method** We used a new colour VEP procedure in 30 headache-free patients suffering from migraine with and without aura and 30 control subjects. We assessed VEPs obtained with reversal achromatic (black-white and grey-black) and chromatic (blue-black and red-black) checkerboard patterns in these subjects.

**Results** A mild longer P1 latency was observed in migraine patients than in control subjects when high contrast achromatic stimulations were used (black-white). This delayed response was statistically significant in migraine with aura (MA) patients ( $p<0.05$ ) when compared with migraine without aura (MWA) patients and control subjects. The responses obtained with red-black chromatic pattern reversal stimulations were delayed in migraine patients when compared with control subjects ( $p<0.01$ ). This delay, however, was more marked in MWA than in MA ( $p<0.05$ ). Interestingly, the P1 latencies obtained in migraine patients with blue coloured pattern reversal stimulations were significantly prolonged than those obtained in control subjects ( $p<0.001$ ) in both MA and MWA patients.

**Conclusion** Our observations suggest that in MA there is a dysfunction of the visual cortex that seems to involve both the magnocellular and parvocellular systems, whereas the parvocellular system seems to be more affected in MWA.

P 2151

#### Headache associated with sexual activity: course of the disease and treatment options

A. Frese, K. Frese, S. Schwaag, A. Rahmann, I. W. Husstedt, S. Evers

*Department of Neurology, University of Münster, Münster, GERMANY*

**Introduction** The objective of our study was to characterize the course of idiopathic headache associated with sexual activity (HSA) and to determine treatment options.

**Method** Out of 37 patients diagnosed with HSA between 1996 and 2001, 28 were contacted by phone in 2002 ( $33.2\pm 19.1$  months later) and questioned by a structured interview.

**Results** 17 patients had never suffered from HSA again. Four patients had suffered from a second phase of the disease but were actually free from HSA. 7 patients reported continued attacks of HSA without longer remissions. Out of those 7, only one had frequent attacks occurring with approximately every second sexual activity, the others had rare attacks.

There were no significant differences between HSA type 1 (dull type,  $n=7$ ) and type 2 (explosive type,  $n=21$ ) regarding the course of the disease.

11 patients with HSA type 2 were treated with betablockers (Propranolol=10, Metoprolol=3, mean treatment duration  $5.0\pm 7.4$  months). 10 reported good results, 1 patient stopped the treatment already after two weeks without success. 3 patients had received indomethacin as a short-term prophylaxis. All three reported good results.

**Conclusion** HSA has a favourable outcome and continued complaints are rare. For those with HSA type 2 and frequent attacks, betablockers for prophylaxis or indomethacin for short-term prophylaxis should be used. For prophylaxis, a short course (2 to 6 months) seems adequate because spontaneous remissions of HSA are frequent.

#### P 2152

##### **Comparison of preference for rizatriptan 10 mg tablet vs ergotamine/caffeine in migraine**

H. Göbel<sup>1</sup>, V. Mateos<sup>2</sup>, S. Christie<sup>3</sup>, C. Allen<sup>4</sup>, F. Vrijens<sup>5</sup>, M. Shivaprakash<sup>4</sup>

<sup>1</sup>Kiel Pain Clinic, Kiel, GERMANY, <sup>2</sup>Central Hospital of Asturias, Oviedo, SPAIN, <sup>3</sup>Ottawa Headache Centre, Ottawa, ON, CANADA, <sup>4</sup>Merck & Co., Inc., Whitehouse Station, NJ, USA, <sup>5</sup>Merck Sharp and Dohme (Europe), Inc., Brussels, BELGIUM

**Introduction** Rizatriptan (MAXALT™) is a selective 5-HT<sub>1B/1D</sub>-receptor agonist with rapid oral absorption and early onset of action in the acute treatment of migraine.

**Method** This randomised double blind crossover outpatient study assessed the preference for rizatriptan 10mg tablet to 2 ergotamine 1 mg/caffeine 100mg tablets in 439 patients treating a single migraine attack with each therapy.

**Results** More than twice as many patients preferred rizatriptan to ergotamine/caffeine (69.9% vs 30.1%,  $p \leq 0.001$ ). Faster relief of headache pain was the most important reason for preference, cited by 67.3% of patients preferring rizatriptan and 54.2% of patients preferring ergotamine/caffeine. The co-primary endpoint of pain free at 2h was also in favour of rizatriptan. 49% of patients were pain free 2h after rizatriptan, compared with 24.3% treated with ergotamine/caffeine ( $p \leq 0.001$ ), rizatriptan being superior within 1h of treatment. Headache relief at 2h was 75.9% for rizatriptan and 47.3% for ergotamine/caffeine ( $p \leq 0.001$ ), rizatriptan being superior to ergotamine/caffeine within 30 minutes of dosing. Almost thirty-six percent of patients taking rizatriptan were pain free at 2h and had no recurrence or need for additional medication, compared to 20% of patients on ergotamine/caffeine ( $p \leq 0.001$ ). Rizatriptan was also superior to ergotamine/caffeine in relieving nausea, phonophobia or photophobia, and returning patients to normal function 2h after dosing ( $p \leq 0.001$ ). More patients were satisfied 2h after treatment with rizatriptan (69.7%) than with ergotamine/caffeine (38.6%,  $p \leq 0.001$ ). Both treatments were well tolerated. The most common adverse events after rizatriptan and ergotamine/caffeine respectively, were dizziness (6.7% and 5.3%), nausea (4.2% and 8.5%) and somnolence (5.5% and 2.3%).

#### P 2153

##### **Co-prescription of triptans with other medications: a cohort study involving 240,268 patients**

S. Tepper<sup>1</sup>, C. Allen<sup>2</sup>, D. Sanders<sup>2</sup>, A. Greene<sup>3</sup>, S. Boccuzzi<sup>3</sup>  
<sup>1</sup>The New England Center for Headache, Stamford, CT, USA, <sup>2</sup>Merck & Co., Inc., Whitehouse Station, NJ, USA, <sup>3</sup>The Institute for Effectiveness Research, Bridgewater, NJ, USA

**Introduction** This study examined the rate of co-prescription of triptans available in the US (sumatriptan, naratriptan, rizatriptan, and zolmitriptan) with specified agents with potential for drug interactions.

**Method** A cohort of 240,268 patients receiving pharmacy benefits from Merck-Medco (N=65+M) was followed over a one-year period. This analysis included patients who received at

least two triptan prescriptions during the study (6/00–5/01). 91% of the cohort remained on the same triptan during the study period. “Co-prescription” was defined as any fill for a select medication obtained between the first and last triptan fills during the study period. Mean patient age was 43 (SD +/-11.6) and 82% were female.

**Results** 21% were co-prescribed selective serotonin reuptake inhibitors, reflecting the considerable co-morbidity of migraine and depression. Patients taking triptans were almost never co-prescribed monoamine oxidase inhibitors (0.02%), and co-prescription of ergots was also low (1.45%). Less than 1% (0.45%) received cimetidine while taking zolmitriptan, while 2.7% of patients taking rizatriptan 10mg also took propranolol. While agents unavailable in the U.S. were not evaluated in this cohort, 6% of patients were treated with potent CYP 3A4 inhibitors, which would not be expected to cause any problems with the triptans in the survey. However, such agents are specifically contraindicated for use with one triptan (eletriptan), recently launched in the EU, suggesting that continued vigilance will be necessary to avoid co-prescription of medicines with the potential for producing adverse drug events.

#### P 2154

##### **Do drivers of patient preference for acute migraine therapies cross populations?**

##### **Analysis from the rizatriptan – sumatriptan preference trials**

F. Skobieranda<sup>1</sup>, R. Von Seggern<sup>2</sup>, C. Allen<sup>3</sup>, F. Vrijens<sup>4</sup>, N. Bohidar<sup>1</sup>, F. Guerra<sup>1</sup>, A. Kolodny<sup>1</sup>

<sup>1</sup>Merck & Co., Inc., West Point, PA, USA, <sup>2</sup>Headache Wellness Center, Greensboro, NC, USA, <sup>3</sup>Merck & Co., Inc., Whitehouse Station, NJ, USA, <sup>4</sup>Merck & Co., Inc., Brussels, BELGIUM

**Introduction** Migraine therapy endpoints now include broad patient-centered measures such as preference, satisfaction, and health-related quality of life. These measures reflect the unique impact of a given disease state (presumably independent of the patient population) and the value system of the patient population (presumably different between populations) and thus may not be generalizable across populations. Patient preference was studied in US and international populations. This descriptive analysis compares drivers of preference between these populations.

**Method** Both studies were randomised, open-label, two-period crossover, multi-center studies. After treatment of both migraines, patients expressed preference by response to an interviewer-administered global preference question. Patients were then asked to choose the *single most important reason for preference* (SMIRP) from a 15-item list of potential drivers of preference.

**Results** 374 US and 381 international patients treated two migraines and expressed preference. Of these groups, 372 US and 314 international patients declared a SMIRP. The most commonly selected SMIRP was faster pain relief chosen by 49% (rizatriptan) and 53% (sumatriptan) of US patients and 57% (rizatriptan) and 53% (sumatriptan) of international patients. No other single determinant was chosen by more than 14% of the US patients and 12% of international patients in either treatment group. Rizatriptan was preferred over sumatriptan in both studies.

**Conclusion** By a wide margin, the speed of headache relief was the most important driver of preference for both populations. These results suggest that this driver of patient preference crosses patient populations, and supports the generalizability of preference as a valuable clinical endpoint in migraine.

## P 2155

**Efficacy and safety of eletriptan versus naratriptan for the treatment of a single migraine attack: results of a multi-center, randomised, placebo-controlled comparative trial**A. E. MacGregor<sup>1</sup>, G. Garcia-Ramos<sup>2</sup>, B. Hilliard<sup>3</sup>, J. Hettiarachchi<sup>3</sup><sup>1</sup>The City of London Migraine Clinic, London, UNITED KINGDOM, <sup>2</sup>Fundación Clínica Médica Sur, Mexico City, MEXICO, <sup>3</sup>Pfizer Pharmaceuticals Group, New York, NY, USA

**Introduction** In previous clinical trials, eletriptan has been found to be more effective than sumatriptan and Cafergot<sup>®</sup><sup>1,2</sup>. This study compared the efficacy and safety of oral eletriptan (40mg) to oral naratriptan (2.5mg) and placebo in treating a single migraine attack.

**Method** Randomised patients (n=483) received eletriptan 40mg (n=192), naratriptan 2.5mg (n=199) or placebo (n=92) in a double-blind, double-dummy parallel-group study. Patients treated one moderate or severe migraine headache during the 12-week study period. The primary efficacy endpoint was 2h headache response.

**Results** Eletriptan 40mg achieved significantly higher headache response than either naratriptan or placebo at 2h (56%, 42% [ $P<0.01$ ], and 31% [ $P<0.0001$ ]). Eletriptan was also superior at 1h (34%, 25% [ $P<0.05$ ] and 21% [ $P<0.01$ ]) and 4h (80%, 67% [ $P<0.01$ ] and 44% [ $P<0.0001$ ]). Pain-free rate at 2h was higher for eletriptan (35%, 18% [ $P<0.0005$ ] and 19% [ $P<0.005$ ]), and eletriptan patients had higher functional status at 2h than naratriptan or placebo (60%, 50% [ $P<0.05$ ] and 44% [ $P<0.0005$ ]). Sustained relief at 24h was higher for patients using eletriptan (38%, 27% [ $P<0.05$ ] and 19% [ $P<0.01$ ]) as were sustained pain-free rates (22%, 11% [ $P<0.01$ ] and 12% [ $P<0.05$ ]). Adverse events (AEs) were generally mild or moderate with similar incidence of all-causality AEs among the treatment groups. Eletriptan had significantly higher treatment acceptability ( $P<0.0005$ ) and 24-hour global evaluation ( $P<0.0005$ ) than naratriptan or placebo.

**Conclusion** Eletriptan 40mg has higher efficacy and acceptability than naratriptan 2.5mg or placebo in the treatment of acute migraine.

**Literature**

1. Goadsby PJ *et al* (2000). *Neurology*; **54**:156–163.
2. Diener H-C *et al* (2002). *Eur Neurol*; **47**:99–107.

## P 2156

**Efficacy of eletriptan in treatment of acute migraine in patients unsuccessfully treated with NSAIDs: results of an open-label study**R. Macalintal-Canlas<sup>1</sup>, S. Lim<sup>2</sup>, Y. C. Chia<sup>3</sup>, S. Wang<sup>4</sup>, Y. M. Cheong<sup>5</sup>, J. Denaro<sup>6</sup>, J. Hettiarachchi<sup>6</sup><sup>1</sup>Makati Medical Center, Legaspi Village, Makati, PHILIPPINES, <sup>2</sup>Singapore General Hospital, Singapore, SINGAPORE, <sup>3</sup>University Malaya Medical Centre, Kuala Lumpur, MALAYSIA, <sup>4</sup>Taipei Veteran General Hospital, Taipei, TAIWAN REPUBLIC OF CHINA, <sup>5</sup>Pfizer Pharmaceutical Group, Selangor, MALAYSIA, <sup>6</sup>Pfizer Pharmaceuticals Group, New York, NY, USA

**Introduction** Although their efficacy has not been well documented, nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for acute and prophylactic treatment of migraine. Therefore the benefits of acute treatment with eletriptan, a selective 5-HT<sub>1B/1D</sub> agonist, were examined in patients inadequately treated with NSAIDs.

**Method** In a 12-week open-label study, subjects (n=113) who had an inadequate response to NSAIDs for two of the last 3 consecutive migraine attacks or who could not tolerate NSAIDs treated a single migraine attack with eletriptan 40 mg.

**Results** At 2 h post dose, eletriptan 40 mg achieved headache response in 66% of subjects (95% CI, 55–77%) increasing to 87% at 4 h (95% CI, 80–95%). Eletriptan improved functional response in 70% of patients at 2 h (95% CI, 59–81%) and 82% at 4 h (95% CI, 73–92%). Migraine recurrence did not occur in most patients (76%; 95% CI, 65–87%). When present at baseline, the associated symptoms of migraine were largely relieved at 2 h including nausea (59%; 95% CI, 45–73%), photophobia (70%; 95% CI, 57–84%), and phonophobia (67%; 95% CI, 53–82%). Most subjects considered their migraine symptoms improved and resumed normal activities faster with eletriptan. Adverse events were generally mild or moderate and transient. Eletriptan was highly preferable and acceptable to NSAID users with 71% of subjects satisfied with treatment.

**Conclusion** Eletriptan 40 mg was effective, highly acceptable and well tolerated in the treatment of migraine pain and associated symptoms amongst subjects who were unsuccessfully treated with NSAIDs.

## P 2157

**Eletriptan: dose-response relationship for efficacy within the clinical dose range**T. Steiner<sup>1</sup>, D. Dodick<sup>2</sup>, J. Hettiarachchi<sup>3</sup><sup>1</sup>Imperial College, London, UNITED KINGDOM, <sup>2</sup>Mayo Clinic Scottsdale, Scottsdale, AZ, USA, <sup>3</sup>Pfizer Pharmaceuticals Group, New York, NY, USA

**Introduction** Eletriptan demonstrates linear pharmacokinetics within its clinical dose range of 20–80mg<sup>1,2</sup>. This analysis evaluates a dose-response relationship for efficacy of eletriptan in acute migraine therapy based on standard outcome measures: 2-hour headache response and pain-free rates and sustained headache-response and sustained pain-free rates.

**Method** First-dose, first-attack data were pooled from 7 phase III randomised, double blind trials of similar design comparing eletriptan 20mg (E20, n=434), 40mg (E40, n=1918) and 80mg (E80, n=1444) with placebo (n=1055). “Headache response” (reduction to mild or no pain) at 2h was sustained if it became no worse (i.e., no recurrence) in 24 hours without further medication. Pain-free outcomes required no pain at 2h and (if sustained) no recurrence or further medication in 24h.

**Results** Headache response and pain-free rates at 2h were: E20 50% and 16%; E40 60% and 27%; E80 66% and 33%. Sustained headache response and pain-free rates showed similar and statistically significant ( $P<0.0001$ ) dose-related increases: E20 30% and 11%; E40 44% and 21%; E80 48% and 25%; all 3 doses of eletriptan were significantly ( $P<0.05$ ) superior to placebo (14% and 4%) on these measures. Recurrence rates were inversely dose-related ( $P<0.0001$ ): E20 28%; E40 23%; E80 21%.

**Conclusion** Eletriptan 20–80mg shows efficacy in the acute treatment of migraine headache, which is clearly dose-related across this therapeutic range. Clinicians may use this to patients’ advantage, titrating the dose to meet their individual needs.

**Literature**

1. Shah AK *et al* (2002). *J Clin Pharmacol*. (in press)
2. Milton KA *et al* (2002). *J Clin Pharmacol*. (in press)

P 2158

**A randomised, double-blind, placebo-controlled, parallel-group evaluation of sumatriptan 50mg and 100mg tablets administered during the mild pain phase of a menstrually associated migraine attack.**M. Ilmavirta<sup>1</sup>, J. V. Loftus<sup>2</sup>, D. Boswell<sup>2</sup><sup>1</sup>Medical Research Centre Toritutkain Ltd, Jyvaskyla, FINLAND, <sup>2</sup>GSK, Greenford, UNITED KINGDOM

**Introduction** Retrospective and prospective studies show that sumatriptan 100mg tablets are effective and well tolerated in the treatment of menstrually associated migraine (MAM), measured by pain reduction from moderate/severe, to mild/none. Recent data shows that sumatriptan taken at the mild pain phase produces a higher response rate.

**Method** The objectives of this study, conducted in 12 countries worldwide, was to determine the efficacy of sumatriptan 100mg (primary) and 50mg (secondary) in MAM by measuring the percentage of subjects with complete pain relief 2 hours after treatment. Migraine sufferers reporting regularly occurring MAM and whom experience moderate/severe MAM pain preceded by mild pain were eligible. Subjects were randomised in a 1:1:1 ratio to treat one MAM within 3 months, ideally within one hour of onset of mild pain.

**Results** Complete relief at 2 hours was achieved by: 22% (29/132) taking placebo, 58% (77/133) taking sumatriptan 100mg, ( $p < 0.001$  versus placebo), and 51% (71/138) taking sumatriptan 50mg, ( $p < 0.001$  versus placebo) in the primary endpoint population and 27% (17/64) taking placebo, 73% (49/67) taking sumatriptan 100mg, ( $p < 0.001$  versus placebo), and 62% (34/55) taking sumatriptan 50mg ( $p < 0.001$  versus placebo) in subjects dosing within one hour of mild pain (per protocol population,  $n=187$ ) AE's in the sumatriptan 100mg, 50mg and placebo treated groups were 20%, 13% and 6% respectively. No SAE's occurred.

**Conclusion** Sumatriptan 100mg and 50mg tablets were effective and well tolerated in the treatment of MAM. Additionally, the results add to the evidence that early treatment during mild pain increases efficacy.

P 2159

**Efficacy of eletriptan and zolmitriptan in the treatment of acute migraine: Results of a comparative, placebo-controlled study**H. Massiou<sup>1</sup>, T. J. Steiner<sup>2</sup>, H. Diener<sup>3</sup>, J. Schoenen<sup>4</sup>, N. Muirhead<sup>5</sup>, C. Sikes<sup>5</sup><sup>1</sup>Hôpital Lariboisière, Antony, FRANCE, <sup>2</sup>Imperial College, London, UNITED KINGDOM, <sup>3</sup>University Essen, Essen, GERMANY, <sup>4</sup>University of Liège, Liège, BELGIUM, <sup>5</sup>Pfizer Pharmaceuticals Group, New York, NY, USA

**Introduction** This study compared eletriptan 40mg and 80mg with zolmitriptan 2.5mg and placebo.

**Method** In a double-blind, double-dummy, parallel-group, placebo-controlled study, 1337 patients were randomised to receive eletriptan 80mg (E80;  $n=396$ ), eletriptan 40mg (E40;  $n=392$ ), zolmitriptan 2.5mg (Z2.5;  $n=405$ ) or placebo (PBO;  $n=144$ ) for one migraine attack. In vitro dissolution testing and a formal bioequivalence study demonstrated bioequivalence of zolmitriptan tablet and capsule.

**Results** Results are presented for E80, E40, Z2.5 and PBO, respectively. Headache response rates were 74%, 64%, 60% and 22% at 2h ( $P=0.0001$ , E80 vs. Z2.5) and 40%, 28%, 25% and

5% at 1h ( $P < 0.0001$ , E80 vs. Z2.5). E80 and E40 were superior to PBO at both time points ( $P < 0.0001$ ). At 30 min, E80 was superior to Z2.5 (12% vs. 7%;  $P < 0.05$ ). Two-hour pain-free rates were 44%, 32%, 26% and 6% ( $P < 0.0001$ , E80 vs. Z2.5). Headache recurrence rates within 24h were 33%, 29%, 38% and 52%. Post-hoc analysis showed sustained response rates at 24 h of 47%, 44%, 35% and 11% ( $P < 0.001$  E80 vs. Z2.5,  $P < 0.01$  E40 vs. Z2.5,  $P < 0.0001$  eletriptan vs. PBO). E80 was superior to Z2.5 for sustained pain-free rate (29% vs. 17%;  $P < 0.0001$ ). Adverse events were generally mild or moderate and transient with the most common being asthenia (8%, 3%, 3%, 0%) and nausea (4% all groups). Both eletriptan doses were rated more acceptable than Z2.5.

**Conclusion** E80 has significantly greater efficacy at 2h than Z2.5 in the acute treatment of migraine. Both eletriptan doses are superior to Z2.5 over 24h as assessed by sustained response and patient acceptability.

P 2160

**Significant 1-hour pain-free rates with zolmitriptan 2.5 mg orally disintegrating tablet in treatment of migraine: results of a large double-blind, placebo-controlled trial**M. M. Tuchman<sup>1</sup>, E. Spierings<sup>2</sup>, S. Abu-Shakra<sup>3</sup>, W. Wasiewski<sup>3</sup><sup>1</sup>Palm Beach Neurological Center, Palm Beach Gardens, FL, USA, <sup>2</sup>Brigham and Women's Hospital, Boston, MA, USA, <sup>3</sup>AstraZeneca, Wilmington, DE, USA

**Introduction** The objective of our study was to evaluate the clinical efficacy of zolmitriptan 2.5 mg orally disintegrating tablets for the acute treatment of migraine.

**Method** This was a 25-center, randomised, double-blind, placebo-controlled, parallel-group, 2-attack study (608 adult migraines; 304 per treatment group). The ITT populations 281 in the zolmitriptan group and 284 in the placebo group who treated at least one mild, moderate or severe migraine attack (90% of the zolmitriptan and 87% of the placebo group treated 2 attacks).

**Results** Zolmitriptan 2.5 mg orally disintegrating tablet showed superior efficacy to placebo in achieving a pain-free status at 2 hour (primary endpoint): zolmitriptan 40% vs. 20% of placebo group ( $n=535$  and 530 attacks, respectively;  $p < 0.001$ ). Pain-free response rates were superior to placebo starting at 1 hour (zolmitriptan 13%, placebo 8%,  $p < 0.01$ ), and at 1.5 hrs (25% vs. 14%;  $p < 0.001$ ). Significantly more patients in the zolmitriptan group achieved sustained pain-free rates (31%) vs. placebo (14%;  $p < 0.001$ ). Zolmitriptan 2.5 mg was well tolerated and AEs considered treatment-related were reported by 25% of patients in the zolmitriptan 2.5 mg group and 10% in the placebo group.

**Conclusion** Achieving pain free status is now considered an ideal measure of treatment efficacy in migraine. This study is one of the few clinical trials to prospectively study pain-free response rates in headaches of any severity as a primary endpoint. Zolmitriptan 2.5 mg orally disintegrating tablet demonstrated high pain-free rates vs. placebo as early as 1 hour after treatment.

Supported by AstraZeneca, LP.

## P 2161

**Treatment of mild migraine with oral zolmitriptan 2.5 mg provides high pain-free response rates and prevents progression to more severe migraine in patients with significant migraine-related disability**

C. Lucas<sup>1</sup>, J. A. Klapper<sup>2</sup>, Ø. Røsjø<sup>3</sup>, A. Poole Jørgensen<sup>4</sup>, T. Soisson<sup>5</sup>, B. Charlesworth<sup>6</sup>

<sup>1</sup>Hospital Salengro, Lille, FRANCE, <sup>2</sup>Colorado Neurology and Headache Center, Denver, CO, USA, <sup>3</sup>Private Practice, Oslo, NORWAY, <sup>4</sup>Sjølyst Medisinske Senter, Oslo, NORWAY, <sup>5</sup>Lariboisere, Paris, FRANCE, <sup>6</sup>AstraZeneca, Macclesfield, UNITED KINGDOM

**Introduction** Preliminary evidence from post-hoc analyses and open-label studies indicates that treatment in the mild phase of a migraine provides higher pain-free rates. This is the first prospective controlled study to assess pain-free response in the treatment of mild migraine.

**Method** 302 patients with migraine attacks that typically commence mild but progress to moderate/severe intensity, and with moderate or severe migraine-related disability, were randomised to oral zolmitriptan 2.5 mg or placebo for the treatment of a single migraine attack in the mild phase. The primary endpoint was 2-hour pain-free response rate. Time to headache progression was one of the secondary endpoints investigated.

**Results** 280 patients were included in the ITT population. Zolmitriptan was associated with significantly higher pain-free response rates compared with placebo at 1.5 (29.4% vs. 14.2%) and 2 hours (43.4 vs. 18.4%) post-dose. This response was even more marked in patients who treated early: in the zolmitriptan group, 56.6% of patients who treated a mild migraine within 15 minutes of headache onset were pain free at 2 hours compared with 20.0% of placebo recipients. Oral zolmitriptan prevented progression of migraine from a mild to a more severe attack within 2 hours of treatment in a significantly greater number of patients than placebo (46.3% vs. 29.6%;  $p=0.0064$ ).

**Conclusion** In patients who typically experience significant migraine-related disability, treatment of migraine in the mild phase with oral zolmitriptan 2.5 mg produces high pain-free response rates and significantly reduces the progression of mild migraine to more severe headache compared with placebo.

## P 2162

**Zolmitriptan formulations provide fast relief in the acute treatment of migraine**

B. Charlesworth, R. Yates

AstraZeneca, Macclesfield, UNITED KINGDOM

**Introduction** Patients who suffer from the debilitating symptoms of migraine need fast, effective pain relief.

**Method** In a randomised placebo-controlled study 656 patients were treated up to 2 moderate/severe attacks with zolmitriptan 5mg ODT or matching placebo.

**Results** The conventional zolmitriptan tablet was significantly more effective than placebo in patients with menstrually-associated migraine from 30 minutes after dosing.<sup>1</sup> Similarly, the zolmitriptan orally disintegrating tablet (ODT) has been shown to be effective from 30 minutes after treatment. In a randomised placebo-controlled study of 656 patients treating up to 2 moderate/severe attacks with zolmitriptan 5mg ODT or matching placebo, the headache response rate at 30 min was 16.5% for

zolmitriptan vs 12.5% for placebo ( $p<0.05$ ). In a separate study, the zolmitriptan ODT 2.5mg tablet produced at least a 1-point improvement in headache pain intensity at 30 mins post-dose (22% vs 15%;  $p<0.05$ ). Zolmitriptan nasal spray has an even faster onset of action. Pharmacokinetic data have shown that zolmitriptan is detectable in the plasma as early as 5 minutes after nasal administration. In a multicentre, double-blind study, headache response for zolmitriptan nasal spray 5mg showed a significant difference compared with placebo from 15 mins after treatment (10.6% vs 5.1%, respectively).

**Conclusion** Patients can be assured that whichever formulation of zolmitriptan they choose will provide fast, effective relief from migraine. The zolmitriptan conventional tablet and the ODT have a 30 min speed of onset and the nasal spray formulation works even faster (within 15 mins).

**Literature**

<sup>1</sup>Loder L, et al. (2002). Oral Zolmitriptan Exhibits Efficacy as Early as 30 Minutes in Menstrually Associated Migraine: Results of a Large Multicenter Placebo-Controlled Study. *Neurology* 58 (7) Suppl 3: s 55.002.

## P 2163

**Migraine, triptan treatment and the risk of cardiovascular disease, stroke and mortality**

G. C. Hall<sup>1</sup>, M. M. Brown<sup>2</sup>, J. Mo<sup>3</sup>, K. D. MacRae<sup>4</sup>

<sup>1</sup>Grimsdyke House, Barnet, UNITED KINGDOM, <sup>2</sup>University College, London, UNITED KINGDOM, <sup>3</sup>Pfizer inc., New York, NY, USA, <sup>4</sup>University of Surrey, Guilford, UNITED KINGDOM

**Introduction** It is unknown whether the reported increased risk of stroke and chest pain with migraine is associated with triptan use. The aim of this study is to evaluate the incidence of cardiovascular outcomes, stroke and mortality in a migraine cohort, stratified by triptan treatment.

**Method** A retrospective cohort study of 63,575 subjects with migraine recorded in the UK General Practice Research Database, grouped into triptan “users” and “non-users”. Controls were matched by age, sex and practice.

**Results** Triptans were less frequently prescribed to the young, elderly, males and those with cardiovascular and cerebrovascular risk factors. Adjusted hazard ratios (HR) showed a statistically significant increased risk of stroke (1.51, 95% CI 1.26–1.82) and ischaemic heart disease excluding MI (IHD) (1.24, 95% CI 1.09–1.41) in “non-users” but not in “users” (1.13, 95% CI 0.78–1.65 for stroke; 1.22, 95% CI 0.96–1.53 for IHD). Decreased risk of all-cause mortality (HR 0.72, 95% CI 0.65–0.80) was observed in “non-users”. Of those classified (33%), the risk of ischaemic (HR 2.49, 95% CI 1.62–3.83) but not haemorrhagic stroke (HR 1.34, 95% CI 0.90–1.99) was significantly increased. Observed HRs for “users” and “non-users” respectively were 0.93 (95% CI 0.60–1.42); 1.11 (95% CI 0.91–1.36) for myocardial infarction (MI), 0.99 (95% CI 0.58–1.68); 0.83 (95% CI 0.66–1.03) for cardiovascular mortality.

**Conclusion** These data suggest that triptan therapy is not associated with increased risk of cardiovascular disease, stroke, or mortality. No association was found between migraine and MI or cardiovascular mortality. The association in “non-users” between stroke and migraine and the hypothesis that lower mortality results from confounding by socio-economic status needs investigation.

P 2164

**Ultrasonography in migraine diagnosis**

I. Melnichuk

*Ukrainian State Medical University, Kiev, UKRAINE*

**Introduction** Migraines are the second most common form of primary headaches, affecting approximately 10 to 15% of the global population during their most productive years. This condition frequently impacts the migraine sufferer's quality of life.

**Method** The correct diagnosis of migraines is based on the International Headache Society's (IHS) diagnostic criteria from 1988, a careful clinical history, and neurological examinations. Based on a study involving 22 migraine patients, only 3 of them had aura, which consists of: difficulties in speech, blurred vision, and numbness in the face and one hand. During their migraine attacks, 21 of the patients had an Ultrasonography migraine pattern. This consisted of: 1) a high level of lineal velocity blood in the sinus durae matter collateral to the side of the head, and 2) asymmetrical measurements consisting of more than 30%, in the bloodstream, in supratrochlearis arteries. Only 1 patient had a high level of lineal velocity blood in the sinus durae matter. This can be explained in the presence of a different phase of the migraine attack. The other Ultrasonography (US) criteria was normal in the other patients.

**Conclusion** My suggestion is that we use Ultrasonography (US) for the visualization of migraine attacks and that we include Ultrasonographic images in the probable critiquing of migraines.

P 2165

**Migraine and patent foramen ovale on transcranial Doppler**

I. Domitrz, J. Mieszkowski

*Department of Neurology, Medical Academy, Warsaw, POLAND*

**Introduction** Pathomechanism of migraine and migraine aura is unknown. Migraine has been reported as possible risk factor for ischemic stroke. The relationship between migraine and stroke is stronger in patients suffering from migraine with aura (MA) compared to those in whom aura does not accompany the migraine attacks. Some authors reported coexistence of migraine and patent foramen ovale (PFO). The aim of our study was to evaluate the frequency of PFO in patients with migraine with aura and compare it with the prevalence of PFO in healthy age-matched control group.

**Method** We assessed 38 patients (30 females and 8 males) suffering from migraine with aura and 50 controls (28 females and 22 males). In order to detect PFO the contrast transcranial Doppler was performed during Valsalva manoeuvre.

**Results** The prevalence of PFO was found in 18 of 38 patients with migraine with aura (47%) compared to 11 of 50 control subjects (22%). The difference between MA patients and control patients was statistically significant ( $p=0.0077$ ).

**Conclusion** These findings suggest that at least some attacks of migraine with aura may be due to paradoxical embolism.

P 2166

**Increased neuromuscular excitability in migraine patients: a concomitant sign or an association with latent tetany?**

J. Opavsky

*Faculty of Physical Culture, Palacky University, Olomouc, CZECH REPUBLIC*

**Introduction** The study was focused on the detection of the clinical signs of an increased neuromuscular excitability in migraine patients due to a described association between migraine and tetany.

**Method** 42 subjects (40 women and 2 men, mean age of 40.5 years) with the diagnosis of migraine with or without aura, repeatedly followed-up during the last 2 years, underwent a neurological examination focused on the signs of an increased neuromuscular excitability. In all of them, the presence of the Chvostek's sign (CS) and in 28 of them, the presence of the Tromner's sign (TS) were assessed. The CS and TS have been frequently detected in subjects with tetany.

**Results** A repeatedly positive CS was proven in 28 of the subjects under study (66.6%). An inconstant presence of this sign was detected in 5 subjects (12%). A repeatedly positive TS was proven in 15 of 28 subjects (53.6%). An inconstant presence of this sign was detected in 3 subjects of this subgroup (10.7%). Repeated, as well as inconstant common occurrence of these two signs was registered in 13 of 28 subjects (46.4%).

**Conclusion** The frequent detection of the positive CS and TS in the subjects under study is consistent with the hypothesis of hyperexcitability in migraine. For migraine patients, special attention should be given to these clinical signs of an increased neuromuscular excitability and it is recommendable to carry out a biochemical study focused on magnesium and calcium metabolism and EMG ischaemic test for the detection of tetany.

P 2167

**Evaluation of lipid peroxidation representing oxidative stress in patients with migraine**Y. Altunkaynak<sup>1</sup>, M. Ozturk<sup>1</sup>, V. Sozmen<sup>1</sup>, N. Erdal<sup>2</sup>,E. Altunkaynak<sup>2</sup>, F. Ismen<sup>2</sup>, S. Baybas<sup>1</sup><sup>1</sup>*Bakirkoy State Hospital for Neurologic and Psychiatric**Diseases, Istanbul, TURKEY, <sup>2</sup>Taksim State Hospital, Istanbul, TURKEY*

**Introduction** Lipid peroxidation represent typically oxidative stress. The cellular damage caused by free radicals in biological systems implied oxidative stress plays an important role in the etiopathogenesis of migraine. In this study, to determine oxidative stress/antioxidant state profile in patients with migraine during attacks and interictal periods, we evaluated the levels of the substances reacting with tiobarbituric acid representing lipid peroxidizing products (TBARS), and uric acid and albumin representing extracellular antioxidant systems.

**Method** The study group consisted of 26 female (mean age  $32\pm 8.57$ ) and 13 male (mean age  $32.28\pm 10.15$ ) patients migraine and equal number of healthy subjects with the same gender distribution and mean age. Parametric student-t, Wilcoxon matched and Spearman correlation were used for statistical analysis.

**Results** The initial and attack serum levels of TBARS in patient group were  $3.85\pm 0.49\mu\text{M}$  and  $4.75\pm 0.64\mu\text{M}$  respectively. The initial and attack serum levels of uric acid in the patient group were  $4.15\pm 0.89$  and  $3.89\pm 0.89$  mg/dl respectively. The initial and attack serum levels of albumin in the patient group were  $5.0\pm 0.29$  and  $4.95\pm 0.33$  mg/dl respectively. The serum levels of TBARS in the patient group were significantly higher than the control group globally ( $p<0.001$ ). Comparison of TBARS values during initial and attack periods revealed TBARS levels were significantly higher during attack periods ( $p<0.001$ ). Uric acid levels were significantly lower during attack period ( $p<0.001$ ). Albumin levels were not significantly different in two groups ( $p>0.05$ ).

**Conclusion** Conclusively, the TBARS levels are significantly higher during initial and attack periods in the patients with migraine and this result shows lipid peroxidation rises in the patients.

P 2168

**The effects of exercise on migraine headache and its relationship with blood nitric oxide level**

S. Osun Naryn<sup>1</sup>, L. Pinar Yanicodlu<sup>1</sup>, D. Erhap<sup>2</sup>, V. Öztürk<sup>1</sup>, F. Ydyman<sup>1</sup>

<sup>1</sup>Department of Neurology, Izmir, TURKEY, <sup>2</sup>Department of Neurology, Ankara, TURKEY

**Introduction** The purpose of this study is to observe the effects of moderate level aerobic exercise program on migraine attacks.

**Method** Besides the medication of migraine, a moderate level of aerobic exercise program, 3 times a week for 1 hour, was provided to randomly selected 20 classical migrainous women; while 20 similarly subjects received only medical therapy.

**Results** At the end of 4 months therapy, although the pain severity, frequency and duration in both group decreased significantly; the "Visual Analogue Scale Scores" showed that, exercised group benefited from the therapies more than non-exercised group. Also "Pain Disability Index", and "Gutmann Scale Scores" which are criteria of the "life quality" of the subjects, showed, a significant relief in the exercised group; compared to non-exercised and only medically treated group. After the treatment period of 4 months; a significant increase of serum nitric oxide (NO) levels in exercised group, but not in the non-exercised group was detected.

**Conclusion** These results support previous reports about "possible coupling between exercise and endogenous NO formation". The physical fitness scores of the exercised subjects comparing to non-exercised controls, might help to explain the beneficial effects of physical exercise and NO formation to cardiovascular benefits, besides the pain reduction and stress relevant.

P 2169

**Middle cerebral artery hemodynamic changes following CO<sub>2</sub> inhalation, nitroglycerine and sumatriptan**

D. Russell<sup>1</sup>, R. Brucher<sup>2</sup>

<sup>1</sup>Rikshospitalet, Oslo, NORWAY, <sup>2</sup>University of Applied Sciences, Ulm, GERMANY

**Introduction** The aim of this study was to assess blood flow and cross-section area index changes following CO<sub>2</sub> inhalation, nitroglycerine and sumatriptan using transcranial Doppler (TCD).

**Method** 5 healthy subjects (aged 26–54 years) took part in the study. Frequency-weighted first moment calculations of Doppler power were used to calculate blood flow indexes using specially designed software (BR02) and these arbitrary values were calibrated off-set to 0 flow. Cross-section area (CSA) indexes were calculated by dividing the calibrated blood flow indexes by the maximum velocities. Accuracy of this method has been assessed in an in vitro closed loop study. In 5 subjects CO<sub>2</sub> was inhaled via a mask in a concentration which was gradually increased to 8% during 6 minutes. 3 of the subjects were given 1 mg nitroglycerine sublingually and 3 subjects were given 12 mg sumatriptan subcutaneously. TCD monitoring was continuously carried out on the left MCA from 5 minutes before to 30 minutes after these procedures.

**Results** Blood flow indexes (increases from 50–100%) and maximum velocities showed a linear relationship during CO<sub>2</sub> inhalation, whereas the CSA indexes remained almost constant in all five subjects (mean±1 SD, 99±2.2%). Nitroglycerine administration in 3 subjects caused CSA index increases of 25, 17 and 29%, whereas sumatriptan in 3 subjects caused CSA index decreases of 24, 13 and 12%.

**Conclusion** In this study of healthy subjects using TCD we found that MCA blood flow indexes and velocities showed a linear relationship during CO<sub>2</sub> inhalation whereas MCA cross-section area indexes remained approximately constant. Nitroglycerine, on the other hand, caused a vasodilatation of the MCA and sumatriptan an MCA vasoconstriction. These results suggest that this method should now be assessed in more extensive clinical studies.

P 2170

**Depressive symptoms in headache subtypes**

G. Gesztelyi<sup>1</sup>, D. Bereczki<sup>2</sup>

<sup>1</sup>Neurology and Headache Outpatient Clinic, City Health Service of Debrecen, Debrecen, HUNGARY, <sup>2</sup>Department of Neurology, University of Debrecen, Debrecen, HUNGARY

**Introduction** The efficacy of antidepressants in primary headaches and the role of serotonin both in migraine and in depression imply that depression and primary headaches might be related.

**Method** 183 consecutive patients with primary headaches (migraine, tension-type headache and cluster headache), or cervicogenic headache and sciatic pain were enrolled in 2 neurological practices. The frequency, duration and severity of the headache/pain and disease duration were recorded by a standard questionnaire. Severity of depressive symptoms was evaluated by the 21-item Beck Depression Inventory (BDI).

**Results** Mean age of the patients was 40.4±12.7 years. Mean BDI scores were 10.8±8.2 in migraine (n=46), 14.9±11.7 in tension-type headache (n=46), 14.5±10.3 in cervicogenic headache (n=43), 15.0±10.1 in patients with sciatic pain (n=19), and 19.2±14.6 in a heterogeneous group with combined headaches (n=28). Data of the single patient with cluster headache is not presented. In the total group BDI score depended on pain frequency (Spearman R=0.27, P=0.0002) and severity (Spearman R=0.25, P=0.0008). Although migraine patients had the lowest BDI score, there was no statistically significant difference among patients with migraine, tension-type headache, cervicogenic headache and sciatic pain (P=0.27, Kruskal-Wallis ANOVA). When a multiple regression model was used including headache subtype, age, frequency and severity of pain and disease duration, again, only pain frequency (P=0.00002) and severity (P=0.003) emerged as significant predictors of the severity of depressive symptoms.

**Conclusion** Severity of depressive symptoms in headache patients is determined rather by the frequency and severity of the pain than by the subtype of the headache.

P 2171

**The necessity of C2 ganglionolysis in select patients for the treatment of cervicogenic headaches**

S. Kamran

Hamad General Hospital, Doha, QATAR

**Introduction** The aim of this study was to evaluate the effectiveness of C2 ganglionolysis for chronic headaches.

**Method** We previously reported 52 patients undergoing cervical RFTC for cervicogenic headaches. Patients were selected by



Sjaastad criteria underwent cervical facet injections with at least 80% headache relief. Those who did not obtain headache relief were included in this study. These patients underwent diagnostic greater occipital nerve block (GO). Selected patients underwent RFTC of C2 (C2 ganglionolysis). Patients were followed for 6 months with headache days per month and VAS pre and 6 months post treatment. One interventional procedure was performed.

**Results** 10 patients were included in the study. The headache involved retro auricular and retro orbital locations. (n=6) reported partial (50%) and (n=4) no headache relief after first RFTC. (n=10) reported 100% headache relief with GO block. These patients underwent C2 ganglionolysis (unilateral 7, bilateral 3). All reported complete headache relief while on the table. Pre-treatment headache days /month 4 to 12 (average 7), VAS 4 to 8 (average 6) was reduced to headache days /month 0 to 1 and VAS to 0 to 2, at 6 months. No complications were reported.

**Conclusion** C2 headache when mixed with CH is difficult to separate. These patients may not obtain any or partial relief with medial branch RFTC. A complete headache relief with GO block followed by C2 ganglionolysis can obtain complete headache relief. However, on clinical basis were not able to determine when the C2 ganglionolysis was necessary. A larger study is underway to answer further questions. The C2 ganglionolysis is a safe and effective technique.

#### P 2172

##### Oxcarbazepine prophylaxis for chronic headaches

J. Krusz<sup>1</sup>, R. B. Nett<sup>2</sup>

<sup>1</sup>Anodyne PainCare, Dallas, TX, USA, <sup>2</sup>San Antonio Headache Institute, San Antonio, TX, USA

**Introduction** We wanted to study a new anticonvulsant agent that has blocking effects on sodium and calcium channels, and inhibition of glutamate release. These actions are found in other agents that have been shown to be useful in treating chronic migraines and other headaches.

**Method** 85 patients were selected for add-on or initial therapy with open-label oxcarbazepine from 2 headache clinic populations. Patients had chronic migraine headaches that had failed at least one, and often 2 or more, neuronal stabilizing agents (n=65). Average number of migraines per month was 7.8, with 12 additional tension-type headaches per month. 35 had co-existent chronic neuropathic pain. Oxcarbazepine was started at 150mg per day and slowly titrated to maximal effect. Patients kept headache diaries and rated severity on a 0 to 10 scale.

**Results** 46 patients responded to oxcarbazepine treatment with 38 reporting greater than 50% reduction in migraine frequency and 8 with 25–50% reductions. 4 patients with chronic daily headache had resolution of their headaches. 10 patients did not respond and 6 discontinued due to side effects; 3 were lost to follow-up. 20 patients have just been started. Average dose was 1450 mg per day in 2 doses. Remaining migraines in responders were at least 30% less severe (0 to 10 scale).

**Conclusion** This open-label study with oxcarbazepine shows very good efficacy in a difficult to treat population of refractory migraine and tension-type headache patients. It is at least as effective as other neuronal stabilizing agents that have been tried for similar populations. It would be warranted to perform double-blind studies with oxcarbazepine in the prophylaxis treatment of migraines and other headache syndromes.

#### P 2173

##### Chronic paroxysmal hemicrania with sensory disturbances in the distribution of the trigeminal nerve: a presentation of 3 cases.

S. Sabetay<sup>1,2</sup>, B. Weller<sup>1,2</sup>, Y. River<sup>1,2</sup>

<sup>1</sup>The Department of Neurology, Bnai-Zion Medical Center, Haifa, ISRAEL, <sup>2</sup>The Technion School of Medicine, Haifa, ISRAEL

**Introduction** Chronic Paroxysmal Hemicrania (CPH) is an episodic disorder with facial pain and autonomic disturbance.

**Method** We present 3 patients fulfilling criteria for the diagnosis of chronic paroxysmal hemicrania, including the positive response to Indomethacin treatment.

**Results** Our patients had distinct sensory disturbance in the distribution of the ipsilateral trigeminal nerve (particularly the ophthalmic branch) during the attack. Imaging studies of the brainstem were negative. On 2 patients we performed the blink reflex test (repetitive and single stimulation) on the affected side and contralaterally. During the attack, we obtained prolonged time interval for the R2 wave bilaterally following stimulation of the affected side. In addition, we found loss of attenuation of R1 & R2 on repetitive stimulation.

**Conclusion** As known so far, chronic paroxysmal hemicrania syndrome does not involve facial sensory disturbance. Our observation indicates a possible role of the pontine tegmentum in generating the pain, sensory loss, and associated autonomic manifestations. It is perhaps the first series of patients in the medical literature with CPH and episodic trigeminal sensory loss.

#### P 2174

##### "Symptomatic" migraine: case report

A. Roceanu, G. Iana, O. Bajenaru

Emergency University Hospital, Bucharest, ROMANIA

**Case report** A 45 year old woman was admitted to the Department of Neurology of the University Hospital of Bucharest following an extremely severe left-sided temporo-occipital throbbing headache, accompanied by visual disturbances, nausea and vomiting.

She had a 6-year history of such attacks of unilateral headache preceded most of the time by visual positive (phosphenes) or negative (scotomas) phenomena, which started specially in the right visual hemi-field and sometimes migrate across the visual field. Since then, she was labelled as migraine with aura.

For the last 6 months she noticed an increase in frequency and also in the duration and intensity of these attacks and their lack of response to the usual medication (non-steroidal anti-inflammatory drugs, antiemetics). There was no family history of migraine.

Physical and neurological examination on admission disclosed a slight papilloedema and a right Babinsky sign which warranted an imaging procedure. A cerebral computed tomography showed a left-sided occipital arteriovenous malformation which was confirmed by a cerebral angiography.

**Conclusion** About 10–12% of the population are migraine sufferers, and routine CT scanning is too expensive for a screening headache evaluation to a patient with normal physical and neurological examination. A careful history with correct interpretation of the patient diary, a thorough physical and neurolo-

gical examination may raise the suspicion of "symptomatic" migraine due to associated structural cerebral lesions and the indication for neuroimaging procedures.

## P 2175

**Idiopathic intracranial hypertension without papilloedema**

M. Moghaddasi<sup>1,2</sup>, A. Freydoonnejad<sup>3</sup>, B. Zamani<sup>2</sup>

<sup>1</sup>Rasool Akram Hospital, Tehran, ISLAMIC REPUBLIC OF IRAN, <sup>2</sup>Iran University of Medical Sciences, Tehran, ISLAMIC REPUBLIC OF IRAN, <sup>3</sup>Ministry of Petroleum Main Hospital, Tehran, ISLAMIC REPUBLIC OF IRAN

**Introduction** Idiopathic intracranial hypertension (IIH), also known as pseudotumour cerebri, (1,2) is characterized by headache, papilloedema, minimal or absent focal neurologic sign and normal CSF findings, all occurring in the absence of enlarged ventricles or an intracranial mass on CT scanning or MRI. (1,3) Pseudotumour cerebri has a number cause or pathogenetic association, (4) but the most common form of the syndrome has no firmly established cause – i.e. it is idiopathic and is now generally referred to as idiopathic intracranial hypertension. (2)

**Case report** A 45-year-old woman was referred with complaint of headache 5 months prior to admission. Headache described as a dull and a feeling of pressure lasting a few hours a day and 3–4 days a week. It was mainly localized in occipital and radiating to frontal region as an occasion. It was pulseless occasionally with nausea without vomiting. There was no photophobia or phonophobia and no more complaint except for transient diplopia. Past medical history was negative for systemic disease such as hypo or hyperthyroidism, hyperparathyroidism, Cushing disease etc. Some medication such as Brufen, Inderal, Surmontil, Triptysol and Sodium valproate was given in last few months with no improvement. On arrival: BP=130/90, RR=18, PR=78, Wt=105 kg. Systemic physical examination was normal. In neurological examination mental status was normal, cranial nerves exam including fundoscopy, Snellen visual acuity and confrontation perimeter were all normal except for right abducens paresis. Brain MRI with and without GD was normal. Lumbar puncture was performed and showed: CSF pressure=400 mm H<sub>2</sub>O, WBC=0, RBC=5, protein=15mg/100, sugar=55mg/100 (concomitant blood sugar=95), Gram stain and sedimentation for malignant cell were negative. Laboratory testes such as CBC, PBS, ESR, TFT, ANA, ANCA, RPR, PPD were all normal.

Patient was diagnosed as IIH and underwent lumbar puncture every other day. The patient's headache gradually subsided and diplopia improved. After five successive LP, the CSF pressure fell to 200 mm H<sub>2</sub>O and the patient was discharged with Acetazolamide 250 mg tds. Two weeks later the CSF pressure was 240 mm H<sub>2</sub>O and after 3 alternate day lumbar puncture, the CSF pressure fell to 190 mm H<sub>2</sub>O and the patient discharged with Acetazolamide.

**Conclusion** IIH in its classic form present with headache and papilloedema that raised the suspicion of hydrocephalus or tumours, when brain imaging showed normal size ventricles without evidences of a mass lesion and subsequent lumbar puncture showed only raised of CSF pressure, then it is called pseudotumour or IIH. Although papilloedema is a cardinal feature of IIH, but in rare cases it may occur without papilloedema, (3) or pseudopapilloedema, (5) therefore it is advised that in the presence of obesity and chronic headache, a spinal tap may be indicated to exclude the presence of IIH without papilloedema.

## P 2176

**The effectiveness of prophylactic treatment of sertraline on headache and neuropsychological parameters of menstrual migraine patients**

A. Erdemoglu<sup>1</sup>, O. Oguzturk<sup>2</sup>

<sup>1</sup>Kirikkale University, Ankara, TURKEY, <sup>2</sup>Kirikkale University, Kirikkale, TURKEY

**Introduction** The aim of the study was to investigate the effectiveness of sertraline on headache parameters, depression and anxiety scores of menstrual migraine patients.

**Method** 30 patients, age ranged between 22–35 (mean. 301±1.3), were admitted to the Neurology department between 2001–2002 and were diagnosed as menstrual migraine. 30 healthy age and sex-matched patients were included into the study. Headache frequency, severity and duration were recorded. Sertraline was administered for three months. Zung, Beck Depression tests, STA-I and STA-II tests were performed.

**Results** Mean headache frequency was 3.2±0.6 and 1.1±0.4, mean headache severity 8.6±0.7 and 4.3±1.1 in pre and post treatment, respectively (p<0.01). In pre-treatment, the daily activities were limited in 86% of patients and 43% of patients in post-treatment (p<0.01). The anxiety and depression scores differed between menstrual migraine patients and control group. A significant correlation was observed between the scores of anxiety (p<0.05) and depression (0.04) and headache frequency and severity. The headache parameters, anxiety and depression scores was significantly changed at the end of the study.

**Conclusion** Sertraline is found to be a safe and effective agent in reducing in headache parameters besides anxiety and depression scores of menstrual migraine patients. In treatment of menstrual migraine patients, the level of anxiety and depression should be evaluated and treated properly for optimal results.

## P 2177

**Levetiracetam, given intravenously, for acute intractable migraines**

J. Krusz<sup>1</sup>, D. Daniel<sup>2</sup>

<sup>1</sup>Anodyne PainCare, Dallas, TX, USA, <sup>2</sup>Trinity Pharmacy, Dallas, TX, USA

**Introduction** Levetiracetam, the S-enantiomer of piracetam, blocks high-voltage (N-type) calcium channels. It has been shown, for the first time (Krusz, 2001) to have value in migraine prophylaxis, given orally. We decided to prepare and utilize a sterile intravenous form of this agent for use in treating acute intractable migraines in the headache clinic.

**Method** Sterile, preservative-free levetiracetam, 200mg/ml or 400mg/ml was prepared in a laminar flow hood by a compounding pharmacist (DD). Particulate matter was filtered out through a series of filtrations and the solution was stabilized at a pH of 6.0. The resulting solution was clear. 16 patients with intractable migraine who failed usual abortive therapy at home were seen in the clinic. 2 patients were treated twice with IV levetiracetam. 6 were female and 10 male. Average age was 46.8 years (range 28–58). Headache severity in 2 patients was #5/10 and more than #7/10 in the rest. An IV line was started with normal saline. No other medications were given, orally or IV. A test dose of 400mg levetiracetam was given and then 400–600mg was given every 5 minutes to maximum effect.

**Results** 8 patients had complete resolution of their migraine. Average decrease of severity was 77.2%, at an average dose of 4167mg (range 400–11200mg) over 56 minutes. 1 patient had no response. No side effects were reported by any patient.

**Conclusion** This preliminary open-label study with intravenous levetiracetam in the treatment of migraine shows very good efficacy and is comparable to other available acute IV agents. It is well tolerated over a wide dose range with no toxicity.

P 2178

**Zolmitriptan orally disintegrating tablet is preferred over sumatriptan tablet in acute treatment of migraine**

B. Charlesworth, on behalf of the ZEST study group  
*AstraZeneca, Macclesfield, UNITED KINGDOM*

**Introduction** A zolmitriptan formulation has been developed that dissolves in the mouth without the need for water. This study evaluated patient preference for zolmitriptan 2.5mg orally disintegrating tablet (ODT; Zomig Rapimelt®) or sumatriptan 50mg tablet for acute treatment of migraine.

**Method** Patients meeting IHS criteria for migraine were randomised to zolmitriptan 2.5mg ODT or sumatriptan 50mg tablet to treat a single migraine attack. Patients returned to the clinic within 1 week of treatment and were given the alternate treatment to treat a second migraine attack within 12 weeks.

**Results** Of the 186 patients in the ITT population, 168 treated with both formulations and answered the preference question. Overall, 60.1% of patients preferred zolmitriptan ODT, while 39.9% preferred sumatriptan tablet ( $p=0.0130$ ). A significantly greater proportion of patients felt that zolmitriptan ODT was the least disruptive treatment (83.6% vs 16.4%), was easier to take (85.5% vs 14.5%), was more convenient to take (86.1% vs 13.9%) and enabled them to maintain an active lifestyle (65.5% vs 34.5%) compared with the sumatriptan tablet (all  $p<0.0001$ ). The zolmitriptan ODT was rated as excellent or good by 69.5% of respondents compared with 52% for the sumatriptan tablet. Overall preference favoured zolmitriptan ODT among patients with baseline nausea or vomiting. More than 90% of patients stated that zolmitriptan ODT allows migraine to be treated any time and anywhere.

**Conclusion** A significant majority of adults with migraine prefer zolmitriptan ODT to sumatriptan tablet and consider the zolmitriptan ODT to be convenient and allows treatment any time a migraine strikes.

P 2179

**Intradermal Botulinum toxin, type A, treatment for cervicogenic migraine**

J. Krusz

*Anodyne PainCare, Dallas, TX, USA*

**Introduction** Botulinum toxin, type A, has been used to treat migraine headaches, but the results of past studies have varied and are not always dose-dependent. I chose an intradermal route for this agent, on the basis that nociceptive fibers are most numerous in the skin and that cutaneous sensory input from the cervical region may contribute to migraine headaches.

**Method** 14 patients with IHS-criteria migraine headaches were treated; 12 had failed neck surgery and 10 were primarily unilateral in headache location. 4 had bilateral cervicogenic migraines. All had cervical muscle spasm, evidenced by examination. Botulinum toxin, type A, (100 units) was given intradermally at the site of greater and lesser occipital nerve inlets, on the side of migraine symptoms.

**Results** 9 patients reported decrease in migraine headaches and spasm on the side of intradermal administration. Average decrease in migraine frequency was over 70%, and remaining headaches were 50% less severe. Average duration of toxin effect was 12 weeks (range=5–19 weeks). 3 were treated more

than once, but more than 4 months apart. 3 patients did not respond to treatment, although 1 had cessation of muscle spasm. 2 patients were just injected.

**Conclusion** Botulinum toxin, type A, given intradermally is quite effective in reducing cervicogenic migraines. This new delivery site for the toxin raises speculation about mechanisms of action via uptake into nociceptive fibers with transport to the dorsal horn of the spinal cord. Blockade of pain transmission at central facilitative sites may then occur, as these may contribute to persistent cervicogenic migraines. Double-blind studies with botulinum toxin, type A, to replicate these open-label observations are definitely warranted.

## Ageing and dementia 1

P 2180

**Production of nitric oxide and proinflammatory cytokines by cultured microglia stimulated with heparan sulphate proteoglycan.**

S. Bussini, P. Baron, P. Fratta, S. Sanzone, F. Cogiமானian, M. Tiriticco, E. Scarpini, G. Scarlato  
*Department of Neurological Sciences, University of Milan, IRCCS Ospedale Maggiore, Milan, ITALY*

Heparan sulphate proteoglycan (HSPG) belongs to a family of molecular chaperons that are detected in the b-amyloid protein (Ab) containing lesions of Alzheimer's disease including activated microglia. HSPG is a complex macromolecule consisting of a protein core to which polysaccharide chain (HS) is covalently attached. HSPG appears very early during plaque evolution and is presumably involved in Ab deposition and fibrillogenesis. The effects of HSPG have previously not been investigated in cultured microglia. We therefore examined by RT-PCR and specific immunoassays the production of nitric oxide (NO) and proinflammatory cytokines by cultured primary murine microglia stimulated with different concentrations of HSPG for up to 48 h. We demonstrate that HSPG induced production of tumour necrosis-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) as well as release of high nitrite (NO $_2^-$ ) levels with increased mRNA accumulation of inducible nitric oxide synthase (iNOS) in a dose- and time-related fashion. On the contrary, heat denatured HSPG or HS alone failed to induce both NO production and cytokine release. These data suggest that HSPG, and particularly its core protein, may contribute to chronic microglial activation detected in senile plaques with production of proinflammatory cytokines and free radicals implicated as a causative factor in neurodegeneration associated with Alzheimer's disease. Supported by Ricerca Finalizzata 2000 of the Italian Ministry of Health.

P 2181

**Effects of central amyloid-beta on learning, glial activation, neuronal degeneration and apoptosis in rats**

A. Alvarez, C. Sampedro, R. Cabelos  
*Eurospes Biomedical Research Centre, A Coruña, SPAIN*

Amyloid-beta (AB) accumulates in Alzheimer's disease (AD) brains, and it is thought that AB deposition is a primary cause of the neuronal death and the cognitive impairment occurring in AD patients. Therefore, reduction of AB deposits might constitute a promising strategy to treat or prevent AD.

Here we investigated the *in vivo* effects of AB fragments 1–28 and 1–40 injected into the rat hippocampus: (1) Effects of bilateral AB28 and AB40 injections on the retention of a passive avoidance learning task (PAL): comparison with control and water-injected (Sham) rats; (2) Effects of unilateral AB28 injections on neuronal degeneration and glial (microglia, astrocytes) activation; (3) effects of unilateral AB40 injections on PAL retention and on neuronal loss and apoptosis.

AB injections impaired learning improvement from the acquisition to the retention PAL sessions ( $p < 0.01$  vs. sham). These amnesic effects of AB being more evident for the 1–40 fragment. The central administration of AB induced a significant neuronal loss in the hippocampal CA1 area ( $p < 0.05$  vs. sham), as well as significant increases in the number of profiles immunoreactive for ED1 ( $p < 0.05$ ) and for GFAP ( $p < 0.05$ ) in the hippocampus. Finally, central AB increased the expression of apoptotic figures in the rat hippocampus and brain cortex ( $p < 0.05$ ).

Our results indicate that central AB impairs learning and induces glial activation, neuronal degeneration and apoptosis in the rat brain.

#### P 2182

##### **The locus caeruleus in Alzheimer's disease: a Golgi and electron microscope study**

S. I. Baloyannis, V. Costa, I. S. Baloyannis

*Aristotelian University, Thessalonica, GREECE*

We studied the fine structure of locus caeruleus of ten early cases of Alzheimer's disease in correlation to normal controls. PHF were abundant in the majority of neurons of the locus caeruleus whereas neuritic plaques were rare. Large number of neurons demonstrated a poverty of the rough endoplasmic reticulum and a marked dilatation of the cisternae of the smooth endoplasmic reticulum as well as fragmentation of the cisternae of the Golgi apparatus. Mitochondrial alterations, such as accumulation of osmiophilic material, fragmentation of the cristae and vacuolization were frequently seen. Axonal dystrophy was observed in substantial number of neurons. Loss of dendritic spines and abbreviation of the dendritic arborisation were also seen in the majority of the round and elongated neurons of the locus caeruleus. Unattached spines were rare. Morphological alterations of the axo-somatic, axo-dendritic and axo-axonic synapses were seen in extend and described in detail. Extensive astrocytosis was seen in all parts of the locus caeruleus in correlation with normal controls. Microglial activation and neuronophagia was minimal in correlation with other parts of the brain stem.

Morphometric estimation of the mitochondria, the Golgi apparatus and the synapses in correlation with normal controls emphasised the substantial changes of those organelles in early cases of Alzheimer's disease.

#### P 2183

##### **Dopamine system in Alzheimer's disease and mild cognitive impairment**

F. Giubilei, C. Calderaro, M. Sepe Monti, B. Caronti, F. Marchione, F. E. Pontieri

*Dept of Neurological Sciences University of Rome "La Sapienza", Rome, ITALY*

It is well known that monoaminergic systems innervate cholinergic cells can affect the release of acetylcholine in the cerebral cortex. With regard to this, previous reports suggest a deregulation of these systems in neurodegenerative diseases

such as Alzheimer's disease (AD), especially in term of dopaminergic deficit. Dopamine receptors have been identified in human and rat peripheral blood lymphocytes (PBL) and there is evidence that human lymphocytes synthesize catecholamines. In the present study we investigated changes in the PBL acetylcholine and Dopamine systems in AD and mild cognitive impairment (MCI) by measuring tyrosine hydroxylase and Dopamine beta-hydroxylase immunoreactivity as well as choline acetyl-transferase and acetylcholine esterase immunoreactivity. The study was carried out on 10 AD patients and 10 MCI subjects. Eight healthy subjects, matched for age, were used as a control population.

The mean value of Dopamine beta-hydroxylase immunoreactivity was significantly higher in AD patients with respect to MCI and control subjects ( $0.16 \pm 0.008$ ,  $0.127 \pm 0.01$ ,  $0.117 \pm 0.006$ , respectively;  $P < 0.0001$ ). By contrast, the immunoreactivity for choline acetyl-transferase was slightly decreased in AD patients as compared with MCI and controls ( $0.054 \pm 0.016$ ,  $0.069 \pm 0.024$ ,  $0.071 \pm 0.008$ ). No significant differences were found between patients and controls on tyrosine-hydroxylase and acetylcholine esterase. These data suggest that monoaminergic systems are impaired in AD and that PBL may represent a simple and useful tool to identify this impairment probably also in the early stage of the disease.

#### P 2184

##### **Apolipoprotein-E genotype and psychiatric symptoms in Alzheimer's disease**

M. Santini, F. R. Pezzella, N. Scaldaferrri, R. Antonini, M. Principe

*University "La Sapienza", Rome, ITALY*

**Introduction** Although the epsilon 4 allele of Apo-E is a well-known risk factor for late-onset Alzheimer's disease (AD), the relationship between Apo-E allele status and non-cognitive symptoms is less clear in AD patients. Psychiatric disturbances are very common in these patients and often worsen their functional disability. Therefore, it is interesting to evaluate any phenotypic aspect of Apo-E allele status. We examined the relationship between Apo-E allele status and psychiatric symptoms in AD patients.

**Methods** Apo-E genotype was determined in 121 AD patients (diagnosed according DSM-IV criteria). The clinical dementia rating scale was used to rate the severity of dementia. The presence of behavioural disturbances, depression and psychotic symptoms was assessed using the neuropsychiatric inventory and the geriatric depression scale.

**Results** The following Apo-E genotypes were observed: 4/4 (n=5), 4/3 (n=45), 4/2 (n=4), 3/3 (n=61), 2/2 (n=6). Depression was found in 38% of the demented subjects, 28.1% of them had psychotic symptoms, and 25.6% had behavioural disturbances. After adjusting for age, sex, education and severity of dementia, we found a significant risk for psychosis (OR 5.3; 95% CI 1.8–16.2) in patients carrying the epsilon 4 allele; no significant relationship was found between either the epsilon 3 allele or the epsilon 2 allele and any of the non-cognitive symptoms assessed.

**Conclusion** Our results suggest that differences in ApoE allele status influence the phenotypic expression in AD patients. In particular, the epsilon 4 allele was found to be a significant risk factor for psychosis.

P 2185

**Proinflammatory cytokines in the CSF of Creutzfeldt-Jakob-disease**

K. Stoeck, M. Bodemer, B. Ciesielczyk, K. Körtner, M. Bartl, B. Mollenhauer, S. Poser, I. Zerr

*University of Göttingen, Department of Neurology, Göttingen, GERMANY***Introduction** Creutzfeldt-Jakob-disease (CJD) is a neurodegenerative disease within the central nervous system (CNS).

The starting-point for this investigation was the analysis of the potential role of cytokines following neurodegeneration.

**Methods** Cerebrospinal fluid and serum samples were collected in the framework of the German CJD surveillance study. Concentrations of the interleukins (IL): IL-1 $\beta$ , IL-6, IL-8, IL-12 and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) were determined using commercially available ELISA-test kits.

Tests were conducted in patients with following diagnosis: CJD (n=10), inflammatory diseases (n=11), epilepsy (n=12), of various dementia (n=17) and healthy controls (n=13).

**Results** No measurable amounts of IL-1 $\beta$ , IL-12 and TNF- $\alpha$  could be detected in CSF. IL-6 was detectable in CSF without significant difference between groups.

The investigation of IL-8 showed a significant elevation in CJD (median 24.86 pg/ml, min 4.81 pg/ml, max 54.12 pg/ml) compared to: inflammatory diseases (median 19.81 pg/ml, min 1.80 pg/ml, max 74.23 pg/ml), epilepsy (median 8.58 pg/ml, min 4.82 pg/ml, max 12.04 pg/ml), dementia (median 17.38 pg/ml, min 3.01 pg/ml, max 45.69 pg/ml).

**Conclusions** Only one of five investigated proinflammatory cytokines were elevated in the CSF of CJD. These new findings may be interesting in view of pathophysiological processes involved in CJD following neurodegeneration. A potential utility of IL-8 in diagnosis has to be investigated further. The mechanisms of elevation of IL-8 in CJD are unknown, but an isolate elevation in CJD compared to other dementia suggests a specific role in prion diseases.

P 2186

**Creutzfeldt-Jakob disease: correlation of MRI and clinical findings**B. Meißner<sup>1</sup>, K. Köhler<sup>2</sup>, A. Schröter<sup>3</sup>, B. Mollenhauer<sup>4</sup>, K. Körtner<sup>4</sup>, M. Bartl<sup>4</sup>, S. Poser<sup>4</sup>, I. Zerr<sup>4</sup><sup>1</sup>*University of Göttingen, Göttingen, GERMANY*, <sup>2</sup>*Statistik, Göttingen, GERMANY*, <sup>3</sup>*Neurology, Würzburg, GERMANY*, <sup>4</sup>*Neurology, Göttingen, GERMANY***Introduction** Creutzfeldt-Jakob disease (CJD) is a fatal disease with characteristic neurological features such as rapid progressive dementia, myoclonus, ataxia, and pyramidal and extrapyramidal signs. Although the definite diagnosis of CJD requires neuropathology, the patients often present with a typical EEG and typical cerebrospinal fluid findings such as elevated levels of 14-3-3 proteins. Lately the MRI showing an increase of signal in the basal ganglia on T2-weighted images has also been discussed as a valuable tool in diagnosing CJD, however, until now, this characteristic finding has not yet been correlated with the clinical features.**Material and methods** We studied 239 patients containing 155 ascertained CJD cases for their neurological symptoms and MRI findings. An investigator blinded for diagnosis assessed the MRI.**Results** surprisingly, among the CJD cases, patients without signal increase of the basal ganglia were shown to have a higher frequency of extrapyramidal disturbances (83% vs. 70%).

Differences that are more striking were shown for symptoms such as depression, sensory disturbances and akinetic mutism, which were more frequent among cases without signal, increase as well. Patients with typical MRI findings seemed to have a more aggressive disease course with rapid progressive dementia in an early stage and a shorter disease duration (median 6.7 months and 9 months respectively).

**Discussion** These results suggest distinct CJD phenotypes distinguished by neuroradiology. These phenotypes have still to be examined in regard to pathological lesion patterns and prevailing genotype.

P 2187

**Difference of depressive symptoms in patients with vascular dementia and Alzheimer's disease**

M. T. Janelidze, R. R. Shakarishvili, A. Z. Tsiskaridze, T. G. Vashadze, M. G. Jibladze

*Institute of Neurology, Tbilisi, GEORGIA***Background** Depressive symptoms frequently accompany both vascular dementia (VAD) and Alzheimer's disease (AD). In VAD they are related to damage of frontal-subcortical networks, while in AD genesis of depressive symptoms are unclear.**Objective** One-year follow-up of VAD and AD patients, including comparison of depressive symptoms and cognitive decline.**Design/Methods** 39 VAD (NINDS-AIREN criteria) and 34 AD (NINDS-ADRDA criteria) patients have been followed up for one year. At the beginning two groups were similar due to dementia severity (MMSE), which was mild. Depressive symptoms were analysed according to Hamilton depression scale.**Results** At the beginning incidence (per 100 person-year) of depressive symptoms was 30.6% among VAD and 13.4% among AD patients (p. 0.05). Despite equal antidepressant regime, depressive symptoms persisted in 58% of VAD while in 62.2% of AD patients' improvement was significant. At follow up prevalence of depressive symptoms in VAD patients increased up to 46.4% and in AD group – up to 16%. Comparison of cognitive decline and depressive symptoms in AD patients did not reveal any correlation. VAD patients treated with antidepressants revealed reduced rate of cognitive decline, in comparison to untreated patients. Reduced rate of cognitive decline was similar among antidepressant responder and non-responder patients.**Conclusions** Persistent depressive symptoms are prominent for VAD. Similarity of reduced cognitive decline in antidepressant effective and ineffective patients suggests that cognitive decline in VAD is caused by multiple neurotransmitter systems damage. Even in the absence of antidepressant's effect, in VAD patients they could be used for slowing of cognitive decline.

P 2188

**Optimisation of the diagnosis of Alzheimer's disease and other dementias (OPDAL) – a survey on carers in Europe**G. Waldemar, for the OPDAL Study Group  
*Rigshospitalet, Copenhagen, DENMARK***Introduction** The OPDAL program was initiated to provide guidelines for physicians and other health care professionals for the disclosure of the diagnosis of Alzheimer's disease or other dementia disorders to the patient and the family. The aim of this survey was to collect opinions from carers about the procedure for diagnostic disclosure, about the information presently provided to patients and family carers, and about the information sought by carers.

**Methods** A total of 323 carers, mainly spouses (56%) or sons and daughters (31%) from 11 countries participated in the survey and completed the 42-item questionnaire.

**Results** In 46% of the cases, the physician had disclosed the diagnosis to the family, and not to the patient, and many family carers did not know how to inform the patient. Drug treatment was initiated in 62% of patients in whom an AD diagnosis was established. While most carers were informed about dosing (76%), fewer were informed about efficacy (46%) and side effects (59%). A large part of the carers (46%) found that the information provided to them was insufficient and in many cases, (29%) there was no regular contact with any physician after the diagnostic disclosure.

**Conclusions** The results highlight the need to develop and implement 1) structured guidelines to health care professionals for the information and education of family carers and patients; 2) written information to patients and carers on a number of issues concerning diagnosis and treatment.

#### P 2189

##### **The incidence and risk factors for new-onset dementia within one year after ischemic stroke**

A. Klimkowicz<sup>1</sup>, A. Slowik<sup>1</sup>, T. Dziedzic<sup>1</sup>, R. Motyl<sup>1</sup>, A. Kiełtyka<sup>2</sup>, A. Szczudlik<sup>1</sup>

<sup>1</sup>Department of Neurology, Cracow, POLAND, <sup>2</sup>Department of Epidemiology, Cracow, POLAND

**Background and Purpose** Dementia after stroke may be caused by vascular lesion, but pre-existing degenerative changes can also influence its development. The patients after stroke with co-existing Alzheimer-type pathology need appropriate treatment. The aim of the study was to evaluate the incidence of pre-stroke and new onset dementia within one year after stroke.

**Methods** We evaluated pre-stroke dementia in 250 patients with ischemic or hemorrhagic stroke using the informant questionnaire on cognitive decline in the elderly (IQCODE). Post-stroke dementia was assessed in 220 patients three months after stroke and in 194 patients one year after stroke by means of the neuropsychological tests and/or IQCODE. The DSM-IV definition for dementia was used.

**Results** Dementia was found in 31.4% of stroke patients three months after stroke and in 32.6% of patients one year after stroke. Nine patients (4.6%) who did not fulfil DSM-IV criteria for dementia 3 months after stroke were found to be demented 9 months later. Twelfth percent of stroke patients had significant impairment of cognitive functions detected by IQCODE on admission suggesting pre-stroke dementia.

Logistic regression analysis showed that older age, higher IQCODE score on admission and lower Barthel index on discharge from the hospital but not CT findings increased the risk of new-onset dementia.

**Conclusions** The results suggest dementia appears in about 20% of patients within one year after stroke. About one-tenth of stroke patients have pre-existing dementia. Older age, cognitive decline before stroke and functional disability on discharge are independent contributors to the risk of dementia after stroke.

#### P 2190

##### **Healthcare utilization and costs due to common medical co-morbidities are increased in community-dwelling patients with Alzheimer's disease**

H. Fillit<sup>1,2</sup>, J. W. Hill<sup>1</sup>, R. Futterman<sup>3</sup>, J. R. Lloyd<sup>4</sup>, V. Mastey<sup>5</sup>

<sup>1</sup>Institute for the Study of Aging, Inc, New York, NY, USA, <sup>2</sup>Departments of Geriatrics and Medicine, Mt Sinai Medical Centre, New York, NY, USA, <sup>3</sup>HIP Health Plans, New York, NY, USA, <sup>4</sup>John R. Lloyd Assoc, Benecia, CA, USA, <sup>5</sup>Pfizer Inc, New York, NY, USA

**Introduction** Co-morbid conditions and healthcare costs were analysed for patients with Alzheimer's disease (AD) in a Medicare-Managed Care Organization (MCO), and implications for disease management programs were derived.

**Methods** A retrospective analysis was conducted of administrative data for AD patients (3517) and age-gender-matched controls (17,480) selected from a Medicare-MCO. The prevalence of AD and 16 co morbid conditions identified using diagnostic classifications from the Charlson co-morbidity index were determined.

**Results** The prevalence of AD in the MCO was 3.9%. Annual healthcare costs were \$3706 higher for AD patients than controls. Costs for co-morbid conditions were higher for AD patients: compared with controls with the same conditions. Costs were \$5389 higher for patients with AD and congestive heart failure (CHF), \$7410 higher for AD and diabetes with chronic complications, and \$4404 higher for AD and diabetes without complications. Increased healthcare costs for AD patients were attributable to greater utilization of inpatient and skilled nursing facilities.

**Conclusion** Costs for AD patients in a Medicare-MCO were 1.6 times higher than for controls and significantly higher for 13 of 16 co-morbid conditions examined, including CHF and diabetes. Much of these costs appeared to be related to potentially avoidable hospitalisations. These findings demonstrate the need for early identification and improved care management and treatment of patients with AD who also have multiple co-morbidities in order to improve the quality of care and potentially reduce healthcare costs in frail elderly.

Supported by Pfizer outcomes research.

#### P 2191

##### **Epidemiology of dementia in Tirana – Albania**

J. Kruja, M. Rakacolli, V. Prifti, L. Buda, D. Agolli  
UHC Mother Theresa, Tirana, ALBANIA

Dementia is a syndrome caused by brain diseases, usually with a chronic and progressive course, characterized by the impairment of the cognitive functions and the deterioration of previously acquired intellectual abilities that interferes with social or occupational functioning.

The scientific purpose of the study was to estimate the prevalence of dementia in the city of Tirana.

We have chosen the persons in a randomised way from the municipal register in a determined geographic area of Tirana City. We found 3550 people over 60 years old registered in that area.

The study had two phases:

Phase I: The people were screened at their home by a team of residents of neurology. Every group of residents conducted the interview according to questionnaire (MMSE) and made a simple neurological objective examination. The people, who resulted positive, passed at the phase two.

Phase II: In this phase the target persons were investigated by a senior of the Clinic of Neurology, University Hospital Centre "Mother Theresa", Tirana-Albania, who made the correct diagnosis according to the specific clinical and radiological criteria of dementia. The ICD 10 diagnostic criteria for dementia are applied.

The data were elaborated in the Neuroepidemiology Unit of the Clinic of Neurology.

The study lasted about 6 months.

During the first phase of the study, we screened 3521 people (from 3550 over 60 years old persons from the municipal registers). There were 380 positive (7.75%; 4.83% for males and 11.45% for females) ( $P < 0.001$ ).

P 2192

**Genetic vascular risk score for sporadic Alzheimer's disease: relationship with mini mental state examination performances**

R. Monastero<sup>1</sup>, A. B. Cefalù<sup>2</sup>, M. Mannino<sup>1</sup>, R. Caldarella<sup>2</sup>, G. Lopez<sup>1</sup>, D. Noto<sup>2</sup>, C. Camarda<sup>1</sup>, R. Cammalleri<sup>1</sup>, L. K. C. Camarda<sup>1</sup>, A. Padovani<sup>3</sup>, M. Aversa<sup>2</sup>, R. M. Camarda<sup>1</sup>  
<sup>1</sup>Dept. of Neurology & Rehabilitation, Palermo, ITALY, <sup>2</sup>Dept. of Internal Medicine, Palermo, ITALY, <sup>3</sup>Neurological Clinic, Brescia, ITALY

**Introduction** Recent evidences suggest a strong association between cardiovascular genetic risk factors and sporadic Alzheimer's disease (sAD). We analysed the distribution of methylenetetrahydrofolate reductase (MTHFR), angiotensin-converting enzyme (ACE), endothelial nitric oxide synthase (eNOS), and apolipoprotein E (APOE) gene polymorphism, all vascular genetic risk factors, and sAD.

**Methods** We studied 142 sAD patients (65% women, mean age  $\pm$  SD of 72.0  $\pm$  9.7) with probable AD, and 142 healthy individuals matched for age, sex, and geographical distribution (mean age  $\pm$  SD of 73.3  $\pm$  7.6). Subjects were genotyped for the following gene polymorphisms: MTHFR (C677T), ACE (I/D), eNOS (G894T), and APOE. A genetic vascular risk score (VRS – ranging from 0 to 8), clustering the allele distribution of the 4 polymorphisms, were calculated.

**Results** No significant differences were detected in genotype or allele frequencies for MTHFR, ACE, and eNOS polymorphisms between cases and controls. The frequency of the e4 allele (cases 20.0%, controls 7.0% –  $p < .0001$ ) and e4-containing genotypes was significantly higher in sAD (cases 40.0%, controls 13.2% –  $p < .0001$ ). Regression analyses showed a significant negative relationship between the genetic VRS and the score obtained on the mini mental state examination (MMSE) ( $r = -0.19$ ,  $p = .008$ ).

**Conclusion** Our data suggest that MTHFR, ACE, and eNOS genotypes do not contribute to genetic susceptibility in Italian sAD, and confirm APOE as a major genetic risk factor for AD. Furthermore, our data suggest that a "vascular" polygenic trait, could affect cognitive performances in sAD patients.

P 2193

**Quantitative EEG changes during cognition tasks in patients with cognitive impairment.**

A. A. Vein, C. G. S. Kramer, D. Frijlink, W. M. van der Vlier, A. W. E. Weverling-Rijnsburger, H. A. M. Middelkoop  
 Leiden University Medical Centre, Leiden, NETHERLANDS

The linear changes of ongoing quantitative EEG were studied in elderly subjects with cognitive impairment during five different conditions: two resting conditions (eyes open and eyes closed)

and three cognition tasks (verbal, non-verbal and fluency). Separate analysis of all frequency bands took place. 21 subjects, mean age 75.4 years (SD=7.2) were divided into 4 matched groups: Controls, subjects with subjective memory complaints, subjects with Mild Cognitive Impairment (MCI), subjects with Alzheimer's disease (AD).

The eyes closed resting condition: AD patients showed significant power differences in all frequency bands compared to controls. No statistical difference was detected between other groups and controls. The eyes opened resting condition: only AD patients demonstrated a statistically significant lack of normal EEG reactivity in comparison with the controls ( $p < 0.01$ ). The verbal and non-verbal tasks: MCI and AD patients had comparable significant low reactivity of theta and alpha bands. The MCI subjects showed significant increase in beta 2 and gamma frequencies ( $p < 0.01$ ) when compared to controls. Performance of fluency task showed no significant EEG spectral value differences between the groups. Cognition tasks during ongoing qEEG-registration can be used to reveal significant abnormalities even in cases of subtle cognitive impairment, i.e. in MCI patients.

P 2194

**SPECT studies in vascular dementia**

W. Chudzik, A. Rozej, B. Kaczorowska, H. Chmielewski, J. Blaszczyk  
 Neurological Clinic, Military Academy, Lodz, POLAND

The diagnosis of vascular dementia is very difficult, but new diagnostic methods have made it easier.

The study was performed in 37 patients aged 48–85, mean 67. SPECT and CT were carried out in all patients. The CT showed two and more ischemic lesions in the brain. In the group of patients with dementia classified according to the criteria of DSM-IV, ICD-10, MMS and Hachinsky Ischemia Scale. SPECT was performed with APEX SP 6 HR, produced by Elscint, using a complex of 99m-Tc-ECD.

**Results** Many hypodense lesions were found in all patients with dementia, especially in the temporal and frontal lobes. These results were compared with CT results. Both examinations showed lesions in the same localisation. However, the hypodense lesions in SPECT were bigger than the lesions in CT. SPECT revealed many ischemic lesions, which were invisible in CT.

**Conclusions** 1. SPECT is a more sensitive examination than CT in the diagnosis of vascular dementia.

2. SPECT should be the primary examination in the diagnosis of vascular dementia if the results of CT are negative.

P 2195

**Isotopic studies in fronto-temporal dementia**

W. Chudzik, A. Rozej, B. Kaczorowska, H. Chmielewski, J. Kochanowski, B. Blaszczyk  
 Neurological Clinic and Nuclear Medicine Department, Military Medical University, Lodz, POLAND

**Introduction** 80% of people over 60 years of age suffer from at least one of the diseases connected with ageing of the organism. Often several diseases appear simultaneously quickly leading to death. Of the diseases connected with ageing, dementia syndromes have the most serious effect on personality and social status. Especially Alzheimer's disease with its progressive brain damage deprives man of his most human values of psychical and emotional life, ending with death of a patient.

**Objectives** In CT investigation there is distinct disappearance of frontal pieces. In SPECT investigation considerable degree of handicap ECD perfusion in frontal and temporal lobes localization, often on both sides.

**Methods** Studies were performed by using CT–SHIMADZU SCT-7000T and SPECT–gamma camera APEX SP 6 HR. Patients were examined for two tests: Mini Mental State Scale and Hamilton Depression Scale.

**Material** 11 patients between 49 to 74 years (mean 61.5). Control group: 9 patients aged between 51 and 72 years (mean 61.5). All of these patients were estimated of melting stupefactions by means of psychological tests, Mini Mental State Scale and Hamilton Depression Scale and screening tests to measure the level of depression in patients of higher age.

**Results** In neuroimaging of dementia syndromes, most often lesions are found in frontal lobe and hippocampus. Our MRI studies showed lesions in the frontal and temporal lobes in two cases. These results and further investigations revealed a considerable hypo-perfusion in frontal and temporal lobes. Both methods, SPECT and PUSG-Doppler, permit the estimation of cerebral blood flow (CBF) for each arterial supply area. However, small disturbances of brain perfusion ascertained by SPECT are not revealed by PUSG-D. PUSG-D as cheap, non-invasive method and easily accessible investigation should find use as diagnostic method for patients with CBF disturbances, especially in dementia syndromes.

**Conclusions** 1. In fronto-demential syndromes with frontal lobe atrophy character it is necessary to perform SPECT study for the purpose of settlement of the final diagnosis.

2. Brain SPECT-ECD is the choice study in fronto-temporal dementia.

#### P 2196

##### **The value of visual EEG in patients with dementia of different origin**

E. Rumpf, J. Grossmann, U. Neumann, G. Noisternig  
*Department of Neurology, LKH, Klagenfurt, AUSTRIA*

**Methods** Standard-EEG-recordings from 40 patients with probable dementia, mild/moderate dementia and severe dementia of different origin were studied. The Mini Mental State Examination (MMSE) classified the severity of mental impairment. Thereby the patients were divided in three groups. Group I: 13 patients with MMSE score between 30–24; Group II: 16 patients with MMSE score between 24–17; Group III: 11 patients with MMSE score 16–0.

The EEGs were visually assessed on the following criteria: 1) Dominant alpha frequency (rhythm) occipital; 2) Dominant theta frequency (rhythm) occipital; 3) Other slow frequencies occipital; 4) Presence of theta and/or delta activity local or diffusely spread; 5) Left/right asymmetry; 6) Spikes, sharp waves, triphasic waves; 7) Generalized, bilateral synchronous paroxysmal Delta activity = bursts, short and long runs of Delta; 8) Effect of eye opening; 9) Suppression periods. There also was an overall classification of EEG in normal, slightly abnormal, moderately abnormal and abnormal.

**Results** Normal EEGs were predominant in group I. No normal EEG was seen in group III. In group III even light and moderately abnormal EEGs were absent. With increasing severity of dementia, there also was an increase of EEG abnormalities. If a normal EEG is seen in a patient who seems to be severely demented, the diagnosis of dementia should be questioned and other causes of dementia should be carefully considered.

Beside the appearance of some theta and delta waves, no other

pathological EEG pattern was found in cases with mild dementia. With increasing severity of dementia, there was an increase of theta and delta waves in the occipital regions, an increase of generalized paroxysmal delta activity and also an increase of spikes, sharp and triphasic waves. Suppression periods were only seen in severely demented patients.

Visually analysed EEG appeared to be a cheap and useful tool in the estimation of the severity of dementia.

#### P 2197

##### **Executive functions and declarative memory in patients with Alzheimer's disease**

D. M. Pavlovic, A. M. Pavlovic, A. Savic, V. Ilic, G. Tomić,  
I. Leposavic  
*Institute of Neurology, Belgrade, YUGOSLAVIA*

**Introduction** Memory impairment is a hallmark of Alzheimer's disease. Executive functions are more preserved at the beginning. We correlated these two functions to see to what extent they are independent so that adequate cognitive treatment measures can be applied.

**Methods** We examined 11 patients with early or moderate Alzheimer's disease, 7 females and 4 males, age 59 to 84 years (mean 70.4), all right handed, mean education 14.2 years, with Mini Mental State Examination (MMSE), Wisconsin Card Sorting Test (WCST), Rey Auditive Verbal Learning Test (RAVLT) and Rey Complex Figure (RCF). Statistical analysis was done with Pearson correlation test.

**Results** MMSE score correlated significantly only with RAVLT evocation and recognition ( $p < 0.05$ ). Also, there was significant correlation between RAVLT evocation and recognition ( $p < 0.05$ ) and RAVLT evocation and RCF evocation after 3 minutes ( $p < 0.05$ ). WCST measures of number of categories achieved and perseverative responses did not correlate neither between each other nor with other variables.

**Conclusion** MMSE, RAVLT evocation and recognition and RCF evocation after 3 minutes are all measuring retrorolandic memory function can be used in monitoring the dementia progression. WCST measures are independent variables and measure prefrontal function that is less severely damaged in early Alzheimer's disease and can be used in cognitive treatment to alleviate memory problems.

#### P 2198

##### **Motor activity in patients with vascular dementia or dementia of Alzheimer's type**

P. Kropp<sup>1</sup>, W. Möller<sup>2</sup>, P. Hoßfeld<sup>3</sup>  
<sup>1</sup>*Institute of Medical Psychology, Kiel, GERMANY,*  
<sup>2</sup>*Creutzfeldt-Institute, Kiel, GERMANY,* <sup>3</sup>*Institute of Sports Medicine, Kiel, GERMANY*

**Introduction** There is evidence that enhanced motor activity in dementia improves cognitive symptoms (Tappen et al. 2000). There is only little information about motor activity in demented patients. **Aim** of the study is the development of a method to assess daily motor activity in patients with vascular dementia (VD) or dementia of Alzheimer's type (DAT).

**Methods** Within 14 days all patients (10 males, median age 77 years, 10 females, median age 76 years) wore a step counter from 9 a.m. to 12 a.m. and 4 p.m. to 6 p.m. The patients suffered from moderate dementia according to the Mini Mental State Examination (MMSE, Folstein).



**Results** Daily mean steps in DAT-patients were 7448 (SD: 620, corresponding 3700 meters), in VD-patients 5720 (SD: 740, corresponding 2700 meters). DAT-patients produced more steps than VD-patients:  $t=2.9$ ,  $p<0.05$ .

**Conclusion** In DAT and VD different brain regions are involved. While DAT-patients suffer from degeneration of the endorhinal system, in VD-patients, among other regions, motor areas and are involved.

P 2199

**Motor reaction time in patients with dementia of Alzheimer's type and in vascular dementia**

W. Möller<sup>1</sup>, P. Kropp<sup>2</sup>, P. Hoßfeld<sup>3</sup>

<sup>1</sup>Creutzfeldt-Institute, Kiel, GERMANY, <sup>2</sup>Institute of Medical Psychology, Kiel, GERMANY, <sup>3</sup>Institute of Sports Medicine, Kiel, GERMANY

**Introduction** Motor reaction time in patients with dementia of Alzheimer's type (DAT) and with vascular dementia (VD) is prolonged. Reaction time consists of the interval between stimulus and recognition (motor initiation time) and of the interval between recognition and motor reaction (motor reaction velocity). Aim of the present study is the differentiation of reaction time into motor initiation time and motor reaction velocity in patients with DAT and with VD.

**Methods** 16 patients (8 DAT, mean age: 69 years, 8 VD, mean age: 67 years) took part in the study. All patients suffered from a moderate dementia (MMSE, Folstein). EMG recordings were made from the forearm of the dominant hand. The time between onset of the visual stimulus and EMG activation and the latency between onset of EMG-activity and pushing the reaction key were registered.

**Results** The mean latency between stimulus onset and EMG activation was in DAT-patients: 1742 ms (SD: 120 ms) and in VD-patients: 1789 ms (SD: 110 ms;  $p>0.1$ , n.s.). The movement-time between EMG onset and pushing the reaction key was in DAT-patients: 125 ms (SD: 28 ms) and in VD-patients: 173 ms (SD: 43 ms;  $p<0.05$ ).

**Conclusion** There were no significant differences between stimulus onset and EMG activation in DAT- and VD- patients. But a significantly prolonged motor latency occurred in VD-patients. We conclude that DAT-patients suffer from cognitive functions, while VD-patients suffer from a cerebro-vascular disease, which influences both cognitive and motor functions.

P 2200

**Cognitive deficits in Parkinson's disease**

I. Ribarits, E. Stefanova, M. Mijajlovic, J. Maric, A. Maksimovic, N. Dragasevic, M. Svetel, V. Kostic  
*Institute of Neurology, Belgrade, YUGOSLAVIA*

**Introduction** Patients with Parkinson's disease (PD) manifest a wide spectrum of cognitive deficits during the course of their illness.

**Methods** Twenty non-medicated PD patients (H&Y stage 1, mean age=44.7±1.6); 20 PD medicated patients (H&Y stage 2, mean age=52.3±2.5, mean dose of levodopa=725±92.5 mg); and 20 medicated PD patients (H&Y stage 3, mean age=62.3±3.2, mean dose of levodopa=950.5±125mg) were included in the study. Age and IQ matched groups of normal controls were also included in this study. Attention, visual memory, problem-solving abilities were investigated with tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

**Results** The visual recognition memory problems are evident in PD medicated patients (H&Y stage 3). Paired associated learning was spared in all three groups. In contrast, on a test of spatial working memory, significant impairment was found in both medicated PD groups, in particular in those patients with more severe clinical deficits. However, all three PD groups were impaired on the test of shifting ability. In a series of problems based on "Tower of London" test medicated patients need significantly longer thinking time about planning the solution, but the accuracy solution deficits were only evident in those patients with more severe PD (H&Y stage 3).

**Conclusions** This study suggests that parallel to the motor decline there is a considerable cognitive decline related to the stage of the disease.

P 2201

**Features of clinical and differential diagnosis in early onset of Alzheimer's disease and vascular dementia**

C. Guranda  
*Scientific and Practical Centre of Neurology and Neurosurgery, Chisinau, REPUBLIC OF MOLDOVA*

P 2202

**TCD in dementia syndromes**

W. Chudzik, A. Rozej, H. Chmielewski, B. Kaczorowska, B. Błaszczyk  
*Neurological Clinic, Military Medical University, Lodz, POLAND*