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Cerebrovascular diseases 3

P 3001

Stroke prevention: Age differences in stress coping

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Introduction Aim of this study was to investigate age differences in stress coping within the scope of a stroke prevention program.
Method 1,177 persons participated in a medical-psychological stroke prevention program with examination of the most prominent risk factors and a stress coping questionnaire. Age differences have been explored between 4 age groups by means of H-test and MANOVA.
Results Findings for medical risk factors and sex differences showed accordance with international data. Concerning stress coping, men demonstrated more emotional dismay and distraction. Also, women who cope preferably by means of distraction or alternative reinforcement are of older age. Furthermore, there is a decrease in aggression by ascending age in women. Scores for reaction control attempts, resignation, self-pity and avoidance are also higher in older age.
Discussion A rise in defensive coping styles with increasing age has been observed. Age differences in stress coping are grounded on variations in the life process as well as social, psychological and physiological changes. A modification of the coping patterns especially in emotional dismay, distraction and alternative reinforcement could possibly contribute to a decrease in medical risk factors of stroke.

P 3002

Ximelagatran: a fixed-dose, oral direct thrombin inhibitor for the long-term prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation

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Ximelagatran is a novel, oral direct thrombin inhibitor with predictable dose-linear pharmacokinetics. SPORTIF IV is an open-label, 2-year follow-up of a 12-week, randomised, parallel-group study, SPORTIF II, [1] in patients with nonvalvular atrial fibrillation (NVAF) with at least 1 additional stroke risk factor. Eligible patients received oral ximelagatran 36 mg bid or warfarin (aiming for INR 2–3). Since the start of SPORTIF II, 187 patients have received ximelagatran for the equivalent of 231 treatment years, and 67 patients have received warfarin for the equivalent of 76 treatment years. There have been 2 (0.9%) nonfatal ischaemic strokes in the ximelagatran group and 2 (2.6%) fatal haemorrhagic strokes in the warfarin group. TIAs have been observed in 1 (0.4%) and 2 (2.6%) patients in the ximelagatran and warfarin groups, respectively. Major bleeds have occurred in 2 (0.9%) ximelagatran-treated and 2 (2.6%) warfarin-treated patients. No routine coagulation monitoring has been performed or required with ximelagatran. Five patients have died, including the 2 warfarin-treated patients who had strokes, while 3 patients died in the ximelagatran group: 1 cardiac arrhythmia, 1 brain tumour, and 1 multiorgan failure due to old age. Asymptomatic S-alanine aminotransferase elevation was observed in a few ximelagatran-treated patients, but decreased spontaneously during continued treatment or discontinuation of therapy. These preliminary data suggest that fixed-dose ximelagatran (36 mg bid) shows promise as an effective and well-tolerated oral anticoagulant for the prevention of stroke and systemic embolism, with no need for routine coagulation monitoring.

Reference

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P 3003

The preventive measures of an embolic stroke with the oral form of the sulodexid

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Introduction Sulodexid has a high affinity to an endothelium of vessels and defends it from damage. The present research was attempted with the purpose to learn a capability of reduction of the arterio-arterial embolism after treatment with sulodexid.
Materials and methods The Doppler sonography of cerebral arteries with microembolus monitoring and after a carotid percussions and duplex scanning have been performed. Twenty-four patients with carotid sources of an embolism were inspected with the transcranial Dopplerography multiply – before and after treatment with sulodexid.
Results Before the treatment, the percussions of carotid arteries, usually carried out in the routine examination for an evaluation of collateral circulation, gave the opportunity to register microembolic signals at all of the patients. In all cases of microembolic signals detection, duplex scanning discovered morphological unstable plaques in the extracranial segment of that artery. We watched decreasing of the embolic signals for 16 patients after the 25-days of treatment (with 500 LSU per day). For 8 patients the embolic signals after treatment have vanished.
Conclusion The new protective properties of the sulodexid were demonstrated with the transcranial Dopplerography. For preventive measures of an embolic stroke can be advised the oral-form of the sulodexid.

P 3004

Flow reversal technique for prevention of embolic complications during carotid angioplasty

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Background Reversal of blood flow in the internal carotid artery during stent implantation has been suggested to prevent embolisation of arteriosclerotic debris.
Patients: Carotid angioplasty/stenting under flow reversal was attempted in 42 patients. Diameter stenosis ranged from 60 to 96% (77±10), the length of the lesion ranged from 5 to 25 mm. At least two lesions contained fresh thrombus.
Methods Reversal of blood flow in the internal carotid artery was achieved by occlusion of both the common and the external carotid artery during the procedure using the Arteria™ device. During the procedure, the blood flowing back into the guiding catheter was re-transfused into the femoral vein via a filter.
Results The device could easily be introduced into the common carotid artery. Balloon occlusion of the common carotid artery as well as the external carotid artery was achieved in all patients. The occlusion time ranged between 6 and 37 min (16±10) and was tolerated reasonable in all patients except two, in whom the balloon had to be deflated repeatedly during the procedure. In all patients, angiographic success was achieved without immediate complications. In one patient, a TIA occurred several hours later. Macroscopic debris was found in the filter in 36/42 patients.
Conclusions Flow reversal in the carotid artery for protection of embolism during carotid angioplasty is feasible in the majority of patients. Atherosclerotic debris is kept back very efficiently. If the balloon occlusion is not tolerated, deflating the balloon intermittently can complete the procedure.

P 3005

Complications of long-term oral anticoagulation by phenoprocoumon in a non-trial neurological environment

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Objective To determine the rate of anticoagulant-related haemorrhage seen in neurological non-trial patients treated with long-acting phenoprocoumon.
Methods 104 consecutive patients, who were treated with phenoprocoumon to prevent stroke recurrence, were reinvestigated regarding current treatment regimen and occurrence of complications and restroke.
Results 91 (29 women, 62 men; mean age 53.5±30.5 years) of the 104 patients could be reinvestigated. Indications for anticoagulation were atrial fibrillation in 46.2%, carotid artery disease in 25.2%, and paradox embolism in 13.2% and other reasons in 15.4%. The total number of follow-up years on phenoprocoumon was 207 (mean 2±1 year per patient). In 16.5% of patients, phenoprocoumon was discontinued for accompanying diseases or complications. 2 patients (2.2%) had major intracerebral bleeding, fatal in one patient (0.8%), and 2 patients (2.2%) had major gastrointestinal bleeding resulting in a 1.9% annual rate of bleeding and an implying 0.48% annual rate of fatal bleeding. In 8 patients a restroke occurred (3.9% annual rate of restroke). In 50.3% (±9.2%) of all anticoagulation tests in the group of patients with continued anticoagulation and in 58.9% (±11.7%) in the group of patients with discontinued anticoagulation ($p<0.05$) the desired INR was not achieved leading to adjustment of dosage.
Conclusion The risk of major anticoagulation related bleeding in our cohort in a non-trial setting (1.9%) is not elevated compared to clinical placebo-controlled trials. However, the rate of discontinuation and rate of not achieved desired INR are higher necessitating more patient and practitioner information and more close meshed follow-up to improve anticoagulation treatment.

P 3006

Validation of the optimal heparin bolus dosage in acute ischemic stroke

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Introduction Neurologists may be reluctant to give initial loading of heparin for fear of hemorrhagic conversion in acute ischemic stroke, although it is recommended in acute myocardial infarction or deep vein thrombosis. We compared bolus dosages of heparin to improve the method of loading in acute ischemic stroke.
Methods Patients with acute ischemic stroke were grouped according to the bolus dosages; 20u/kg in-group I (n=50), 30u/kg in-group II (n=34), and 80u/kg in-group III (n=20). Maintenance dosage was the same (17.5u/kg/hr) in all groups. Activated partial thromboplastin time (aPTT) values at 2hr, 4hr, and 6hr after initial bolus were compared. Therapeutic range was defined to be equivalent to heparin level of 0.3–0.7u/ml by anti-Xa assay.
Results 2 hours after initial bolus injection, 60% of the patient's in-group I was in the subtherapeutic range, while all in-group III showed above the therapeutic values. In-group II, 26% had subtherapeutic aPTT values. Achievement rates of the therapeutic range were similar between groups I and II (36% versus 35%). At 4 hr after bolus, the differences between groups I and II were almost negligible. However, 80% of group III remained supratherapeutic. At 6 hr, 48% of group I and 41% of group II had aPTT values in the therapeutic range whereas 50% of group III were still supratherapeutic ($P<0.01$).
Conclusion Our results suggest that initial heparin bolus of 30u/kg is preferable to 20 or 80u/kg, to achieve earlier therapeutic range and to avoid the overshooting of aPTT values.

P 3007

Catheter closure of patent foramen ovale for prevention of recurrent embolic stroke with the CardioSEAL-STARFlex-Occluder: Acute results and follow-up in 83 consecutive patients

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Background Patients with a cryptogenic stroke or TIA and an associated patent foramen ovale are at risk for recurrent embolic events. The STARFlex occluder is a modified CardioSEAL double umbrella device with microsprings attached in alternating fashion between the opposing arms of the umbrella. The microsprings lead to a better apposition of the device arms to the septum.

Methods Since June 1999 catheter PFO closure was attempted with the STARFlex occluder in 83 patients (mean age 48±13). The annual recurrence rate in this high-risk patient group was 21%. An atrial septal aneurysm was present in 27%. Follow-up was performed by transoesophageal echocardiography (TEE) after 1 and 6 months and clinically in 6 to 12 months intervals.
Results The implantation of the occluder was successful in all patients. During follow up routine 1 month TEE (63/79) revealed a thrombus on the device in 5 patients. In two patients, the thrombus was removed surgically together with the device. After 6 months, TEE showed complete closure of the defect in 50/52 patients (96%). No device arm fractures occurred. One minor stroke and no TIA occurred. The annual recurrence rate for stroke and/or TIA was reduced to 1.2%. No further complications occurred.
Conclusion The STARFlex-occluder is suitable for PFO closure, even in complex defects with associated septal aneurysm. PFO closure is effective in reducing the incidence of cryptogenic stroke in patients who do not have another source of their event.

P 3008

Effect of functional electrical stimulation in recovery of hemiplegic upper extremity in patients with unilateral neglect

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Purpose The goal of this research was to evaluate the effectiveness of the treatment program designed to increase functional use of the upper extremity (UE) in stroke patients with hemilateral neglect.
Method The study includes 24 patients (male+/–7 y.o. right-handers, 4–8 weeks after the stroke) with hemineglect syndrome (18 – had right CVAs, 7 – left CVAs). The patients were randomly assigned to experimental (n–14) and control (n–10) groups. Both groups received conventional therapy. The experimental group additionally received functional electrical stimulation (FES) of hemiplegic UE muscles (trapecius, deltoideus, triceps, extensors of the hand) 5 times a week with duration of 50–60 minutes (12 minutes in each position), for 3–4 weeks.
All subjects were measured, at admission and discharge, for hemineglect presence (verbal designation of the upper contralateral extremity, recognition of their own upper extremities, neglect while reading or writing, copying drawings), arm function, arm muscle tone, muscle electromyographic activity, range of motion in the arm joints and daily life activities.
Results The results show that the FES group improved significantly more than subjects of the control group during the treatment period of four weeks according to visuo-perceptual, visuo-motor abilities, arm function and Barthel Index.
Conclusion We did not succeed in completely restoring the arm function and daily life activities in our experimental group, however, in the light of these results FES appears to be a useful treatment modality to improve motor recovery of hemiplegic UE in patients with unilateral neglect.

P 3009

Effects of neuropeptide Semax (ACTH 4–10) in acute ischemic stroke

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Introduction The new drug Semax (synthetic ACTH 4–10) is a neuropeptide with neurotrophic, immunomodulative and anti-ischemic activity, without hormone effects.
Methods and results The double-blind placebo-controlled trial in 200 patients with carotid ischemic stroke (IS) confirmed safety profile of Semax in daily dose 150 mcg/kg for first 5 days after the event. A time-related analysis revealed acceleration of regress of neurological symptoms in Semax group (by the Orgogozo – OSS and the Scandinavian Scales $p<0.01$ vs. Placebo). Evaluation of IS outcome found out a lower 30-days-mortality ($p<0.05$) and a significantly higher proportion of patients with good recovery (by the Barthel index $p<0.01$ vs. Placebo) in Semax group. Semax decreased CSF levels of IL-1b, IL-8 and CRP by d 3, while continuing elevation of these cytokines was detected in Placebo group ($p<0.001$). Marked increase in IL-10, TNFa, TGF-b1, BDNF and bcl-2 in CSF was registered in Semax group ($p<0.01$ vs. Placebo). Significant correlations between the increase in CSF BDNF level and elevation of OSS score ($r=0.52$, $p=0.03$), as well as between the dynamics of CSF IL-10 level and OSS score ($r=0.45$, $p=0.04$) were revealed. Investigations of thiobarbituric-acid-reactive substances and SOD in CSF confirmed anti-oxidant effects of Semax.
Conclusion The trial demonstrated that Semax was safe and could exert positive clinical effects in patients with carotid are due to its neuroprotective properties.

P 3010

Thrombolytic therapy for ischemic stroke in a community-based setting; a retrospective analysis of the impact on an unselected stroke population

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Background and Purpose Thrombolytic therapy is approved in the U.S.A. for treatment of early onset ischemic stroke within three hours of ictus, but remains controversial in Europe. Approval in North America is based on the NINDS trial, but three other trials have cast doubt on the benefit of thrombolytic therapy. In the present study, we sought to investigate the possible impact of thrombolytic therapy in the setting of an unselected Danish stroke cohort.
Methods This retrospective study included 502 unselected stroke patients admitted from a well-defined catchment area over a period of eight months. Patients were admitted regardless of medical or social condition before stroke, hospital treatment and stay was free of charge, and no selection was made as for age, gender, or stroke severity. The most important criteria from the NINDS trial were applied retrospectively on the Danish cohort in a stepwise manner to identify patients that could be eligible for thrombolytic therapy. The percentage of patients who would benefit from thrombolytic therapy was estimated on the basis of the results from the NINDS trial.

Results 8% would be eligible for thrombolysis. 3% would die irrespective of treatment and 2% would achieve full recovery spontaneously. Five patients (1%) would benefit from thrombolytic therapy. In the ideal situation – all patients admitted in due time after stroke – a maximum of 5% of the whole population would have benefited from thrombolysis.
Conclusion This study suggests that only a very small fraction of all stroke patients may benefit from thrombolytic therapy.

P 3011

Efficacy of transvenous PFO-closure in patients with cerebrovascular events

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The role of the patent foramen ovale (PFO) in patients with cryptogenic cerebrovascular events is well documented. Diagnosis is made by transoesophageal echocardiography (TEE) and transcatheter closure being the widely used alternative treatment to drug therapy or surgery.
In 248 adult patients (aged 18 to 71 years) with at least one cryptogenic cerebrovascular event (64% stroke, 46% TIA or PRIND) transcatheter closure was performed.
TEE findings determined the type and size of the device used. For anticoagulation heparin was given for the procedure, antiplatelet therapy for the following 6 months. We successfully implanted 121 Amplatzer PFO occluders (APFO), 81 Cardioseal (CS) and 46 CS-Starflex (CSStf) devices.
There were 3 early complications (device embolisation, early release, undetected perforation of the roof of LA with the guide wire lead to cardiac tamponade 6 hrs after successful implantation, 5 significant venous haematoma). As late complications, there was 1 LA-perforation by the left atrial disc of an APFO with the need of urgent surgery. Late arrhythmias occurred in 5%. Residual leaks and/or an additional lesion after 6 months were trivial in 3 APFO, 10 CS/CSSTF, 4 others have got a second device.
Transcatheter closure of a PFO is effective in terms of closure rate, is preferable to long-time anticoagulation or other drug therapy, its recurrence rate of neurological events is low. Problems may occur in long tunnel like PFOs with late dislocation after immediate correct positioning, or infolding of the device into the tunnel and incomplete contact with the septum.

P 3012

Early biochemical changes during hyperbaric or normobaric reoxygenation after hypoxic damage in cortical brain slices of Wistar rats

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Objective To determine early nucleotide changes after a hypoxic period with respect to whether hyperbaric oxygen compared to normobaric oxygen or room air (at 1 or 2.5 ATA) is used during reoxygenation of brain slices.
Methods After incubating 300µm brain slices from Wistar rats in a modified artificial cerebrospinal fluid (ACSF) at 37°C the specimens were frozen in liquid nitrogen. Purine and pyrimidine nucleotide levels were measured by anion-exchange HPLC of neutralized perchloric acid extracts of brain slice homogenates. After a 30 min preincubation in ACSF gassed with 100% O2 brain slices were encountered either with 5 or 30 minutes of hypoxia via gassing the medium with 100% nitrogen followed by 60 min reoxygenation with 100% O2 at 1 ATA (NBO) and 2.5 ATA (HBO) or with room air at 1 ATA (NBA) and 2.5 ATA (HBA; n=6–8 each).
Results After 5 min hypoxia, NBO and HBO over 60 min both lead to a recovery of all trinucleotides to control level, reoxygenation after a 30 min hypoxic period resulted only in partial recovery irrespective of the used oxygen pressure. Contrastingly administering room air during reoxygenation nucleotide content stayed at hypoxic level with a tendency of worse outcome of HBA compared to NBA.
Conclusion Reoxygenation (at 1 or 2.5 ATA) resulted in a recovery of the nucleotide status after 5 min but only partially after 30 min of hypoxia, whereas room air did not alter the early hypoxia-induced nucleotide decline in brain slices. HBO is not harmful under these conditions.

P 3013

Hyperbaric oxygen treatment in permanent focal cerebral ischemia – effect on infarct volume, microglia and astrocyte expansion

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Objective Hyperbaric oxygen (HBO) is known to increase oxygen supply to ischemic areas and to effect infarct size in focal cerebral ischemia. We investigated the role of single and repetitive HBO-treatment in a permanent ischemia model.
Methods We treated 32 spontaneously hypertensive rats (SHR) after permanent middle cerebral artery occlusion (MCAO) either with hyperbaric oxygen (2.5 atm abs, 100% oxygen, 90 min) or room air (control group, n=8) in a small animal HBO-chamber once starting at 90 min after MCAO (n=8), twice (3h after first treatment, n=8) or 4 times (3, 6 and 24h after first treatment, n=8). All rats were sacrificed at 7 days after MCAO and infarct volume was measured. TUNEL, microglia and astrocyte staining was performed by triple immunofluorescence labelling and evaluated by confocal laser scanning microscopy.
Results A single HBO treatment reduced the infarct volume by 16%, but repetitive HBO-exposure resulted in less pronounced effects (2 HBO-treatments –10%; 4 HBO-treatments +10%) compared to the control group. However, none of these effects was statistically significant. Likewise, there were no significant differences in the number of TUNEL-positive cells between HBO and control animals. However, we observed distinct patterns of microglia and astrocyte distribution in the penumbral zone but not in the infarct core.
Conclusions Repetitively administered HBO-treatment did not induce a significant effect on infarct size and number of apoptotic cells in the infarct core, but we observed striking differences in the spatial activation of microglia and astrocytes.

P 3014

Cerebral embolisation is reduced y performing coronary artery bypass surgery on; "The beating heart"

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Background Coronary artery bypass surgery (CABG) using cardiopulmonary bypass (on-pump surgery) carries a substantial risk for cerebral injury due to cerebral embolisation. This is due to the whole-body inflammatory response, which is induced by the heart-lung-machine, and the fact that cannulation and cross clamping of the ascending aorta produces atheromatous embolisation. CABG performed without cardiopulmonary bypass (off-pump surgery) may therefore lead to a reduced risk of cerebral embolisation and subsequent cerebral injury. In this prospective, randomised study we have assessed the rate of cerebral embolization during off-pump compared to on-pump surgery.
Material and methods Transcranial Doppler (TCD) was used to determine the number of cerebral microemboli in the left middle cerebral artery during coronary artery bypass surgery in 52 patients, of which 29 were carried out off-pump. Clinical, neuroradiological and neuropsychological assessments were also performed one day prior to surgery and again three months later.
Results There was significantly fewer cerebral microemboli in the off-pump group compared to the on-pump group 16 (range 0–131) versus 66 (range 15–274, $p<0.005$). One ischemic stroke occurred in the on-pump group. Neuropsychological impairment (>20% reduction in at least 2 tests) was found in 8 (35%) of the on-pump and 8 (29%) of the off-pump patients.
Conclusion This study has shown that carrying out CABG using the off-pump technique significantly reduces the number of perioperative cerebral microemboli. There was no significant difference, however, in the neuropsychological findings in the two groups which suggests that embolus composition may be as important as the total number of emboli with regard to cognitive outcome.

P 3015

Haemostasis and hydro-ion homeostasis in experimental cerebral ischemia with application of intravenous laser irradiation of blood

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Use of intravenous laser irradiation of blood (ILIB) is considered to be the most effective method of laser therapy in ischemic disturbances.
This study deals with the investigation of ILIB influence with semiconductor laser (SL) with 860 nm wavelengths to hydro-ion homeostasis and haemostasis in normal rabbits and after modelling of local ischemia of brain (LIB).
LIB was made by bilateral occlusion of common carotid arteries under thiopental anaesthesia for 3 hours. SL radiation power of light guide inserted in the otic vein was 2 or 8.5 mW. Rabbits underwent by one 10-min exposure for 5 days. The K^+, Na^+ concentration in blood, brain parts and the level of brain water content were investigated after finishing a laser course. Coagulation tests (platelet count, activated partial thromboplastin time (APTT), prothrombin time, thrombin time (TT), fibrinogen) were studied after the 1st and 5th ILIB procedures.
ILIB with 2 mW provokes hypocoagulation effect and dehydration of brain structure alone with the K^+, Na^+ concentration decreasing in the normal animals. The early postischemic period is characterized by hypercoagulation syndrome, ionic misbalance and oedema in ischemic brain region. ILIB application after modelling LIB contributes for normalizing of brain water content and haemostasis findings compared to the controls (significant APTT, TT increase ($p<0.001$), fibrinogen decrease by 25% ($p<0.01$)). SL radiation with 8.5 mW power results in marked haemostatic activation in all animals.
Thus, positive effect of ILIB by SL radiation manifests with narrow power diapason.

P 3016

Antioxidation of puerarin introduction

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Puerarin is an isoflavone compound isolated from puerarin lobata (wild) ohwi, a Chinese materia medica. In our previous work it was shown that puerarin induced increases in cerebral blood flow and metabolism and relaxation of the cerebral artery and arterioles (1). In the People's Republic of China puerarin as a new treatment for cerebral ischemia has been widely used in clinic (2). We report the effect of puerarin on lipid peroxide (LPO) and superoxide dismutase (SOD) in animals in present study.
Method The antiperoxidation of puerarin was studied by using colorimetric estimation of LPO (mmol/L) and SOD activity (U/ml). Experiments were carried on mice and rabbits. In vitro the LPO of liver of mice and brain of rabbit were investigated under the influence of puerarin. In vivo the SOD activity of blood and brain of rabbit were studied after intravenous injection of puerarin.
Result The results in vitro showed that puerarin could inhibit significantly the content of LPO. The highest inhibition rates were found to be 86.8% and 90.2% in liver of mice and brain of rabbit respectively. The puerarin enhanced the SOD activity obviously. The highest increase of SOD activity in blood and brain of rabbit were found to be 42.3% and 82.1% respectively.
Conclusion The puerarin could reduce significantly the content of LPO in liver of mice and brain of rabbit and enhance the activity of SOD in blood and brain of rabbits.
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P 3017

The effects of cardiovascular risk factors on haemorheological parameters in patients with chronic cerebrovascular diseases

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Haemorheological factors are of significance in the determination of the flow characteristics of blood and in the regulation of cerebral blood flow. In this study the changes of rheological factors; haematocrit (Hct), plasma fibrinogen concentration (cc.), whole blood (WBV) and plasma viscosity (PV), red blood cell aggregation (AI) and deformability and the relationship of car-

diovascular risk factors with these variables were investigated in 297 patients (173 males, 124 females, mean age 60±11 years) with transient ischemic attack (TIA) or chronic phase (>3 months after onset) ischemic stroke (IS), and in 68 healthy volunteers (30 males, 38 females, mean age 36±6 years). All examined rheological parameters were significantly impaired in the cerebrovascular group compared to controls ($p<0.05$–0.0001). Patients with hypertension, hyperlipidemia, smoking habits and alcohol dependence exhibit increased Hct, plasma fibrinogen concentration, WBW, PV and AI compared to normal controls ($p<0.05$–0.0001). In the cerebrovascular group patients with hyperlipidemia and smoking habits, have the most severe rheological disturbances.
In our study, we proved in chronic ischemic CP that haemorheological abnormalities persist long after an acute stroke, and several parameters are impaired simultaneously. Significant correlation could be seen between blood rheological disturbances and cardiovascular risk factors.

P 3018

Coagulopathies as cause of ischaemic stroke in young adults

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Introduction Strokes before age of 45 have different causes comparing to those after 65 and refer to non-atherosclerotic vascular diseases, cardiogenic emboli and haematology abnormalities.
Objective The aim of the study is to investigate the relationship between coagulopathies and stroke in young patients.
Methods Last year we admitted in our department 137 patients with ischemic stroke aged under 45. Patients were questioned about hypertension, cardiac diseases, diabetes mellitus, previous stroke, cervical trauma, migraine attacks, oral contraception, alcohol, smoking and family history of stroke. After physical examination, patients performed:
– blood count, biochemical profile (lipid, immunological).
– Cerebral CT scan,
– electrocardiography, chest X-ray
– Doppler ultrasound
– angiography (if necessary)
– echocardiography
– in selected cases – antiphospholipid antibodies and natural anticoagulants (protein C, protein S, antithrombin III).
Results A group of 8 young patients (6%), with ischaemic stroke were found with coagulation abnormalities: 4 with protein S deficiencies, 2 with protein C deficiencies, 1 with protein C and antithrombin III deficiencies, 2 with resistance to the activate protein C.
Recurrent ischaemic stroke was present to 4 patients, although they have been treated with antiplatelet drugs.
6 patients had coagulopathies combined with other risk factors for ischaemic stroke: 3 with dislipidemia, 1 with high level of anticardiolipin antibodies, 1 with patent foramen ovale, 1 with diabetes mellitus, 3 with immunological abnormalities.
Conclusion Even a rare cause of ischaemic stroke, the coagulation abnormalities must be considered in young patients in order to prevent the stroke recurrence.

P 3019

Significance of embolic mechanism of cerebral ischemic events in the patients with carotid artery disease

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The **purpose** of study was estimation of significance of embolic mechanism of cerebral ischemic events (CIE) in the patients with carotid artery disease (CAD).
Methods We studied 65 special selected patients with CAD. We used transcranial Doppler sonography with detection of microembolic signals (MES) on the device "Sonomed-300" (Russia), and colour-coded carotid duplex on the device "Acuson 128XP" (USA). 37 patients had MES in the middle cerebral artery following ipsilateral carotid artery compression/percussion (evoked microembolism). They had unstable plaques in appropriate carotid artery without thrombosis. Other 28 patients had carotid stenosis (15%–100% of lumen) without evoked/spontaneous microembolism.
Results We detected spontaneous MES during transcranial Doppler monitoring only in 16.2% of the patients with evoked microembolism. All of them had ulcerated plaques. 45.9% of the patients with evoked embolism had the history of CIE. There was a correlation between CIE and MES ($r=0.44$, $p<0.001$). But there was no correlation between CIE and degree of stenosis. Antiplatelet therapy resulted in elimination MES only in unulcerated plaques. In 28 patients with carotid artery stenosis without microembolism, correlation between CIE and occurring of stenosis was not detected, but there was a correlation between CIE and degree of stenosis ($r=0.49$, $p<0.001$).
Conclusions Artery-to-artery embolism is main mechanism of CIE in the patients with CAD. Carotid artery stenosis without microembolism can cause CIE only in conditions of high degree of stenosis. The patients with MES should be treated with antiplatelet agents. If the elimination of MES has not been reached, carotid endarterectomy should be executed.

P 3020

Affecting factors of hemorrhagic transformation in the middle cerebral artery infarctions

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Objective Hemorrhagic transformation (HT) affects treatment and prognosis in patients with acute ischemic stroke. The factors affecting hemorrhagic transformation in infarcts due to occlusion of middle cerebral artery (MCA) stem or branch were investigated.
Material and method Of 412 patients who were followed in our clinic between January 2001 and December 2001 with acute ischemic stroke, 86 patients with occlusion in MCA stem or branch were enrolled in this study. These patients were divided in two groups as with HT (n=35) and without HT (n=51). Age, sex, systemic arterial hypertension, diabetes mellitus, blood glucose level in acute period, renal and liver function tests, systolic and diastolic arterial blood pressure in the acute period, previous cerebrovascular disease, leukoaraiosis, modified Rankin Disability Score (mRDS), stroke subtype were evaluated.

Results High blood glucose level in acute period and presence of leukoaraiosis in cranial computerized (CCT) tomography were detected as risk factors in development of HT. HT was seen more frequently in MCA total infarction than branch infarction. mRDS have gone worse in the group with HT.
Discussion Development of HT in acute ischemic stroke is reported as 10–65%. High blood glucose level in acute period (p=0.015), leukoaraiosis (p=0.015) and size of infarction (p=0.001) in CCT were detected as important predictor in development of HT in our patients. Prognoses are worse in patients with HT than the other group (p=0.014).

P 3021

Role of monoclonal antibodies in pathogenesis of stroke caused by arterial hypertension

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Immune mechanisms are considered to be significant in pathogenesis of stroke caused by arterial hypertension. Stroke is accompanied by affection of neuroglial complex, which leads to neuroimmune failure. Along with necrosis in cerebral tissue neuron's apoptosis is starting. Apoptosis associated with expression of specific receptors Fas/Apo-1 (CD95) is induced by ischemia, proinflammatory cytokines, and neurotransmitters. In our study, level of CD95 in blood of patients in acute period of stroke was determined. 25 patients (mean age of 57.6 years) were examined with determination of amount of lymphocytes typed by FAS-receptors in blood. In all cases in the acute period increased level of lymphocytes with membrane receptors CD95 was found. It was 17.8±8.7%, compared to 1–2% in the norm.
In high severe cases the CD95 level made 26.4±2.97%, in medium severe cases it was 16.6±2.06%, and in mild 10.5±2.6%. The difference between these groups proved reliable.
Thus rising of lymphocytes FAS-receptors level and correlation between apoptotic change level and gravity of the patients condition were found. It suggests participation of monoclonal antigens CD95 in stroke pathogenesis under conditions of immune response development.
Through T-cell receptor FAS the mechanism of apoptosis is started with development of cell-mediated immune cytolysis. Apoptosis development leads to structural degradation of neural tissue in cases of cerebrovascular events. Consequently, determination of high CD95 level can serve as a diagnostic criterion of stroke severity.

P 3022

Ischemic stroke caused by tumour associated hypercoagulabilty

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Introduction Coagulation disorders like bleeding complications or thrombosis are well known tumour-associated complcations. About 30% of all tumour patients die because of coagulation disorders. However, cerebral complications are less known. We report the case of a 60-year-old patient with tumour-associated hypercoagulabilty as well as thrombocytopenia.
Medical history A 60-year-old patient with an adenocarcinoma of the lung was admitted to our hospital with acute right-side hemiplegia. During the last two weeks, he complained about recurrent neurological deficits. The initial CCT showed a former posterior circulation infarct as well as a former lacunar media circulation and an acute media circulation infarct on the left side. Coagulation test revealed a thrombozytopenia (35 G/l), a decreased level for Fibrinogen (121 mg/dl) and highly increased cross-linked fibrinogen degradation products (69.64 µg/ml – 0.49 µg/ml). Antithrombin III and all other Vitamin-K-dependent coagulation factors showed normal levels. Anticoagulation with heparin was started with consequent decrease of cross-linked fibrinogen degradation products. Thrombocytes and fibrinogen increased respectively. However, on the fourth days the patient died of a massive intracerebral haemorrhage.
Discussion Two different mechanisms of tumour-associated procoagulatory mechanisms are known. Malignant cells produce physiological proteins like tissue plasminogen activator, which activate coagulation factor VII. Additionally tumour cells, especially those of adenocarcinomas, produce abnormal proteins with a procoagulatory effect and increase of factor X activity. Both mechanisms finally lead to thrombin activation.
Conclusion Tumour-associated coagulation disorders lead to a complicated imbalance between pro- and anticoagulation and might cause cerebrovascular complications. Therapy must be carefully decided in any case.

P 3023

Thrombophylic state as risk factor for stroke in young adults

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Background Thrombophylic state is presented as increased coagulability decreased of natural coagulation inhibitors and decreased fibrinolytic activity.
Methods and results We investigated 57 stroke patients, from 20 to 49 years old (average 42.02 years), 36 males and 21 females (proven by CT or MRI of brain). We measured platelet numbers, plasma levels of coagulation factors, platelet aggregation to adenosin dyposphat (ADP) or collagen, plasminogen activator inhibitor-1 (PAI-1), activated thromboplastin time (APTT), antithrombin III (AT III), protein C and activated protein C resistance (APCR).
The platelet numbers were normal in all of the patients (average velue-a.v.-234 x10^9/L). The plasma level of fibrinogen was elevated at 40.35% (a.v. 5.03 g/L, control group 2.7 g/L, p<0.01), and coagulation factor II and V were elevated in two patients. The platelet aggregation was increased at 14.03% (a.v. 135%), and APTT was prolonged at 5.25% (a.v. 39.7 sec), suggested possibility of lupus anticoagulant positivity. PAI-1 was elevated at 26.31% of patients (a.v. 5.49 U/ml, at control group 2.67+–0.5 U/ml, p<0.01) as signs of decreased fibrinolysis. AT-III was decreased in one patient (as well as in his father and his son), while protein, C and APCR were normal in all patients. We concluded that increased coagulability (elevated level of fibrinogen) and decreased fibrinolysis (elevated level of PAI-1) were found in our young stroke patients; in significant number; decreased level of coagulation inhibitor (AT-III) was found in one patient; it is a rare disorder, as it was known. The other factors were not exchanged significantly.

P 3024

Modifiable stroke risk factors and options for secondary stroke prevention

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In the Republic of Moldova, stroke is the second most important cause of mortality and leading cause of severe disability. Improved detection of modifiable risk factors could reduce the rate of stroke and recurrent stroke.
The aim of our study was evaluation of modifiable stroke risk factors, and determination of effective directions for secondary stroke prevention.
Our study was performed on a group of 263 stroke patients treated in the Stroke Unit. The following risk factors were evaluated: Hypertension, atrial fibrillation (AF), diabetes mellitus (DM), cigarette smocking (CS), alcohol consumption (AC), obesity, previous stroke and acute myocardial infarction (AMI), rheumatic valvulopathy and vascular stenosis.
Data analysis suggest high rate of hypertension–36.8% and AF-26, 9%, followed by AC-26, 9%, obesity–25.3% and CS–20.6%. 19% of patients had history of previous stroke and AMI. Ratio for DM, vascular stenosis and rheumatic valvulopathy were much smaller 14.2%, 12.6% and 9.5% consecutively. One risk factor has been established in only 22.2% of the patients and 7.9% of the patients were not under any risk factors. The remained patients, 70%, have had an association of complex risk factors such as: HTA- AMI- AF, or HTA with FA, and HTA -obesity and AC.
The main risk factors for stroke are HTA with no other associated risk factors, or in combinations with AMI, AF, and obesity. Subjects with multiple risk factors should be targeted to reduce the overall risk for stroke. Antihypertensive drugs, life style improvement and diet should represent a good prevention in these cases.

P 3025

Neuropsychological findings in asymptomatic carotid artery stenosis

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Introduction Asymptomatic carotid artery stenosis (ACAS) means that one of or both internal carotid arteries are obstructed by plaques or arteriosclerotic lesions and no history of neurological symptoms (amaurosis fugax, transient ischaemic event and cerebral infarction) are presented. The aim of this study was to estimate the cognitive status in ACAS subjects.
Methods We studied 37 subjects with ACAS and 19 control subjects without present internal carotid stenosis, matched for age and education. A selected group of neuropsychological tests (tap attention, memory, language, visual organization ability, visual motor tracking and motor ability) was administered. The questionnaires for depression and anxiety were applied for the patients and controls.
Results The ACAS showed significant cognitive deficit on digit and visual span tasks of Wechsler memory scale revised and on word fluency tests. The ACAS group was significantly slower on motor performance tasks (finger tapping test, Purdue pegboard test) when they were compared with controls. The significant difficulties for subjects with ACAS were shown on visuomotor tracking task (trail making test, form A and B). The increased anxiety symptoms are present in ACAS group in comparison to control subjects according to the Hamilton anxiety rating scale measures.
Conclusions ACAS subjects showed selected cognitive motor and psychiatric deficits in comparison with control subjects. Although deficits were small, these findings suggest that ACAS may predispose to subclinical cognitive impairment. Longitudinal follow-up is required to determine whether subjects with ACAS were determined to develop overt cognitive decline or to distinguish those who are prone to.

P 3026

Positive and negative mood balance in post-stroke depression

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Introduction The relationship of positive and negative mood to each other and to the severity of depression in stroke patients diagnosed with major depressive disorder (MDD) was evaluated DSMIV diagnostic criteria consider only negative mood. Clark and Watson (1991) attributed both high negative mood (NM) and low positive mood (PM) to be associated with depression. NM, they conclude, is associated with various emotional disorders. It was expected that in PSD, PM would correlate with depression severity independent of NM.
Method Subjects were 12 stroke patients with PSD MDD (DSM IV criteria). The Hamilton depression scale (HAM-D) was used to evaluate severity. Mood was assessed with the positive and negative affect Scale (PANAS). A functional assessment of multiple sclerosis (FAMS) questionnaire containing six scales (contentment, emotional problems, mobility problems, pain, cognitive problems and fatigue) was used.
Results There were 7 females and 5 males. Means were: age 54.3 yrs., months since stroke: 5 months, HAM-D, 23.7 points. Correlation between PANAS-PM and HAM-D ($r=-.58$, $p<.05$) showed that greater depression severity is related with lower positive mood. PANAS-NM scale was not correlated with HAM-D severity ($r=.33$, NS). Also, PANAS-PM and PANAS-NM score did not correlate ($r=-.16$, NS) suggesting independence. HAM-D correlated with FAMS variables of pain ($r=.60$, $p<.05$), cognition ($r=.59$, $P<.05$) and fatigue ($r=.61$, $p<.05$).
Conclusion PM is a factor in clinical depression, and it varied somewhat independently from negative mood.

P 3027

Infusion of PK-Merz (amantadine sulphate) in the acute phase of stroke

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Introduction Infusions of amantadine were used in stroke patients substantiated on the experimental and clinical studies of other authors that confirmed that the preparation acts as an antagonist to glutamate, reducing the disturbances of consciousness, increasing vigilance and modulating the glutaminergic system.
Methods and patients Observations were performed at the Stroke Unit of the Latvian Neuroangiological Centre in 65 patients in the acute period of stroke, using Amantadine 500 ml, 55 drops per minute, intravenously, in addition to generally accepted therapy, excluding other neuroprotectors and stimulators. In the control group were 20 patients, receiving only basic therapy. All the patients had disturbances of consciousness and psychomotor inactivity. The criterion for excluding was psychomotor agitation.

Results The infusions of PK-Merz influenced the patients in the acute phase of ischemic and haemorrhagic stroke: more significantly and sooner than in the control group the level of disturbances of consciousness and inactivity, negativism, rigidity and oligokinesia were reduced, the concentration abilities were improved. In 25% of cases the preparation caused psychomotor anxiety of mild or moderate degree for 3–6 hours after the administration, more often only after the first administration. Other undesirable side effects were not observed.
Conclusion The infusion of PK-Merz may be indicated for stroke patients in the acute stage of stroke if decrease in psychomotor activity is present.

P 3028

Activity of piracetam in stroke patients with acute aphasia

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In this study, the effect prognosis of early high dose piracetam treatment in stroke patients with aphasia was evaluated. The study group included 30 patients, and the control group was 12. Piracetam was given to the study group 12 gr IV bolus, 12 gr per day IV for 1–2 weeks, 12 gr per day orally for 2–3 weeks and 4.8 gr per day orally for 4–8 weeks. Aphasia test was included 13 parameters. Neurological situation was evaluated with Orgozozo and Barthel scales. Scales were applied on the 1st, 4th, 8th, 15th day and 1st, 2nd, 3rd month. Both in study and control groups a significant improvement was seen in speaking fluency, understanding simple questions, responding true-false questions, matching test, and naming the objects and colours. The improvement began from the first month only in the study group. Understanding complex questions showed a significant improvement in both groups but a significant improvement was determined from the beginning of the fourth day, only in the study group. Reading fluency, reading and doing written orders, writing in order and calculating arithmetically showed a significant improvement only in the study group. Orgozozo score improvement, which was significant in both groups, was significant from the beginning of the 15th day only in the study group. Barthel score improvement was significant only in the study group from the beginning of the first month. As a result, number of cases was small however; the piracetam group showed an early significant improvement both in neurological and aphasia situation.

P 3029

Choice of preventive antithrombotic therapy regime in the patients with cardiac sources of cerebral embolism in dependence on emboli content

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The **purpose** of study was estimation of emboli content in the patients with cardiac sources of cerebral embolism for choice of preventive antithrombotic therapy regime.
Methods We studied 49 patients with mechanical prosthetic heart valves (MPHV), 13 patients with non-valvular atrial fibrillation (NVAF), 21 patients with infectious endocarditis (IE). We used transcranial Doppler sonography with detection of microembolic signals (MES) on the device "Sonomed-300" (Russia), and transthoracic echocardiography on the device "Acuson 128XP" (USA).
Results Most of cerebral ischemic events in the patients with MPHV and NVAF happened in conditions of inadequate oral anticoagulation (66.7% and 100%, accordingly). There was no correlation between anticoagulation intensity and MES incidence/number. MES in the patients with NVAF were not detected. MES in the patients with IE were detected only in first two months of disease in conditions of friable valve vegetations. Additional antiplatelet therapy in the patients with MPHV and MES resulted in elimination/reduction microembolism in most cases (75%). The MES number was not reduced in 25%. There was no history of cerebral ischemic events in these patients.
Conclusions The embolic material is heterogeneous. There are red thromboemboli in the chamber sources (e.g. NVAF). There are platelet-dependent particles in the valve sources (e.g. IE). There are red and white thromboemboli, platelet aggregates, and gaseous microbubbles in the MPHV. MES have platelet and gaseous origin. The patients with MPHV and with chamber sources should be treated with oral anticoagulants, and the patients with MES – with antiplatelet agents additionally.

P 3030

Mannitol use and outcome in acute stroke: results from the Mures-Uzhgorod-Debrecen Study

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Background The role of mannitol therapy in acute stroke is controversial and clinical practice on its use varies.
Patients and methods We analysed hospital case fatality in a prospective study in stroke patients treated in three centres in the framework of the Mures-Uzhgorod-Debrecen project. In 2 of the centres, mannitol is regularly administered, whereas in one centre it is rarely used. We compared case fatality of mannitol treated and non-treated patients among age groups (0–54, 55–74, 75–95), groups based on the level of consciousness on admission, among major stroke subtypes, and among centres.
Result Data of 984 patients were analysed. Of these 61% were treated with mannitol. Case fatality was 22% and 9% in the mannitol treated and untreated groups ($P<0.001$). We found association between mannitol treatment and fatal outcome in all age groups, in ischemic as well as in haemorrhagic strokes, in alert patients as well as in those with disturbed level of consciousness, and in all 3 centres. When age, disturbance of consciousness on admission and mannitol treatment status were entered together into a logistic regression model, all of them were significantly associated with a decreased probability of survival.
Conclusions This study does not prove that mannitol is harmful if given in acute stroke but emphasizes the need for properly designed randomised clinical trials to decide whether the current practice of routine use of mannitol in patients with acute stroke is justified, should be restricted to subgroups or should be stopped.

P 3031

Hypolipemiant treatment of stroke patients

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An actual problem is to create some therapeutic strategies that are able to show the essential changes of stroke: hyperlipidemias, lipid peroxide system, decreasing of the antioxidant protection, and rheological changes of the blood.
Purpose A good evaluation of the efficiency of hypolipemiants in complex treatment of stroke.
Methods The study was done on 78 patients with stroke, aged 28–68 years (44 women; 34 men). Control group – 32 persons. Stroke has occurred in 62 cases in the territory of carotid artery and in 16 cases in the vertebro-basilar territory.
48 patients from basic group have been treated along with hypolipemiant drug "Lipanor"–"Sanofi" product.
From the entire lipid, system we have been depicted total lipids, total cholesterol, triglycerides, phospholipids, and low-density lipoproteins.
The laboratory investigations were initially made and repeated after 30 days from administration of "Lipanor".
Results According to the results we have seen changes in the studies indices.
In the lipids system these changes were more noticed in case of total lipids, total cholesterol, and low-density lipoproteins, being increased with 25–28%.
The administration of "Lipanor" drug led to decrease of the mentioned indices to control group.
In case of lipid peroxidation system and antioxidant system there occurred essential changes in the activity of catalaza, SOD, the content of malonic dialdehyde and TAA.
Conclusions The dates of the study allow us to conclude that the administration of "Lipanor" in the complex treatment of stroke patients is efficient not only at the clinical level, but also at the pathogenetic one. Normalization of the lipid system changes can be mentioned as an important factor in stroke secondary prevention.

P 3032

Haemorheologic profile changes after intravenous gammaglobulin administration in neurological disorders

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The **purpose** of this study was to investigate the influence of intravenous gammaglobulin administration on haemorheologic properties changes. The haemorheologic properties have been considered to be a main factor influencing the blood flow in microcirculation.
The study was carried out in the group of 10 patients /seven with polyradiculoneuropathy and three others suffering from myasthenia/, who were treated routinely with intravenous gammaglobulin infusions /Sandoglobulin, Sandoz, 24 g a day in the course of 5 days therapy/. The following haemorheologic factors were estimated: relative blood viscosity, plasma viscosity, red cell deformability and erythrocytes aggregation. For rheological examination the microviscosimeter Low Shear 40 /Contraves/ was used. The level of fibrinogen was estimated by means of standard laboratory method. Each patient was examined three times: before treatment initiation, after the first day and at the end of therapy after five days.
At the comparison of first and last measurements a significant increase of plasma viscosity /$p<0.05$/ and red cells aggregation /$p<0.05$/ was found, whereas erythrocyte deformability was significantly improved /$p<0.05$/.
The **result** of this study indicates a potential negative role of gammaglobulin on the blood flow in microcirculation. In turn, the lack of blood viscosity alteration might suggest an existence of a protective feedback mechanism, which has been exemplified by the red cell elasticity improvement.

P 3033

Essential thrombocythemia as independent stroke risk factor – case report

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P 3034

Oxidative stress and intracerebral haematomas

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P 3035

Neurological symptomatology and neuropsychological diagnostics of hypertensive encephalopathy

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P 3036

State of haemostasis system of acute ischemic stroke and chronic ischemic brain disease during semax therapy

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P 3037

Clinical characteristic of dizziness syndrome in vertebrobasilar insufficiency in women with menopause and efficacy of Betaserc

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P 3038

Dramatic recurrence of stroke in-patient with patent foramen ovale (POF) and no atrial septum aneurysm (ASA), considerations about anticoagulation

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Epilepsy

P 3039

Extracellular pharmacokinetics of levetiracetam in rat hippocampus and frontal cortex

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Introduction We have investigated the temporal kinetic interrelationship of levetiracetam in serum and brain extracellular fluid (frontal cortex and hippocampus) following systemic administration of levetiracetam, a new antiepileptic drug. Concurrent extracellular amino acid concentrations were also determined.
Methods A rat model, which allows serial blood sampling and concurrent brain microdialysis sampling, was used. A catheter was implanted in the jugular vein for blood sampling and microdialysis probes were implanted stereotactically into the hippocampus and frontal cortex. Levetiracetam and amino acid concentrations were measured by HPLC.
Results After administration (40 or 80 mg/kg), levetiracetam rapidly appeared in both serum (Tmax, 0.4–0.7 h) and extracellular fluid (Tmax, 2.0–2.5 h) and concentrations rose linearly and dose-dependently, suggesting that transport across the blood-brain barrier is rapid and not rate-limiting. The kinetic profiles for the hippocampus and frontal cortex were indistinguishable suggesting that levetiracetam distribution in the brain is not brain region specific. However, t1/2 values were significantly larger than those for serum (mean range, 3.0–3.3 h vs. 2.1–2.3 h) and concentrations did not attain equilibrium with respect to serum. Levetiracetam (80 mg/kg) was associated with a significant reduction in taurine in the hippocampus and frontal cortex. Other amino acids were unaffected.
Conclusion Levetiracetam readily and rapidly enters the brain without regional specificity. Its prolonged efflux from and slow equilibration within the brain may explain, in part, its long duration of action that has been reported clinically. The concurrent changes in taurine may contribute to its mechanism of action.

P 3040

Malignant glioma within the temporal lobe in the rat brain after kainic acid induced chronic epilepsy: Single case

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Injected subcutaneously into the rats kainic acid (KA, 10 mg/kg) induces epileptic activities and neurochemical and histopathological alterations which show similarities to the clinical and histopathological changes observed in human temporal lobe epilepsy. Recurrence of spontaneous seizures have been reported 6 months after the initial KA-induced convulsions and hippocampal lesions reflect a very severe form of atrophy and sclerosis at 6 months of injection (Baran et al., 1988). The GABAergic activity and somatostatin levels in selected brain regions (cortical and basal ganglia areas) were significantly increased and these alterations could be involved in the development and progression of spontaneous seizures activities. Within KA-treated rats with initial induced convulsions one of KA rat did not develop spontaneous seizures. In this animal a malignant glioma was found within the temporal lobe, mainly located in the amygdala, infiltrating the adjacent entorhinal cortex, the ventral parts of the hippocampus, the claustrum and parts of the striatum. Interestingly, the GABAergic activity was in control range in all analysed brain region, at 6 months after KA. Somatostatin levels were elevated in the hippocampus and a mild increase was found in cingulate and parietal cortices, while in temporal cortex and amygdala/piriform cortex the somatostatin content was markedly decreased. A lack of spontaneous seizures, and a different, moderate pattern of neurochemical alterations observed in the brain of KA rat with a malignant glioma in the temporal lobe would indicate notable network of GABA and somatostatin activities involving seizures development.

P 3041

Analysis of levetiracetam action on calcium channel subtypes of hippocampal neurons

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Introduction The cellular mechanisms of the anti-seizure-activity of new antiepileptic drug levetiracetam (LEV) are not yet identified. We studied, therefore, sensitivity for LEV of different types of voltage-operated Ca2+ channels in isolated rat CA1 pyramidal neurons, aiming to discriminate their possible role in the specific action of this substance.
Methods Whole-cell patch clamp recordings of Ca2+ channel activity of isolated hippocampal CA1 neurons were performed. For the separation of Ca2+ channel subtypes, their selective blockers were used: nifedipine, w-Conotoxin-GVIA, w-Agatoxin and w-Conotoxin-MVIIC for L-, N-, P- and Q-types respectively. HVA Ca2+ currents were elicited by shifting the holding potential from –70 mV to depolarising test potentials for 50ms, and LVA from –80 mV to –45mV.
Results In control cells L-type accounted for 25%, N-type for 45.5%, P-type for 16.8% and Q-type for 9.4%. LEV application irreversibly inhibited the evoked currents in all tested cells. IC50 for the inhibition by LEV of HVA Ca2+ channels was 14.7μM. The maximum inhibition was observed at 200μM and was about 18%. Application of 200μM LEV in the presence of the corresponding selective blockers further reduced the calcium current amplitude by 17.0%, 15.6% and 17.4% for L-, P- and Q-types respectively. However, LEV was ineffective in the presence of the selective blocker of N-type channels. No inhibitory effect was observed on LVA Ca2+ channels.
Conclusions Present study indicates that LEV selectively influences the activity of N-type Ca2+ channels of CA1 pyramidal hippocampal neurons with 37% maximal inhibitory efficacy.
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P 3042

Epileptic focus localization with the EEG: The importance of high spatial sampling

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Introduction EEG/MEG source reconstructions have become a valuable technique to non-invasively localize the epileptic focus. However, precise localization depends on the spatial sampling of the electromagnetic field, i.e. on the number of electrodes/sensors. While several studies with large-array MEG systems exist, EEG studies most often use only standard clinical electrode set-up of maximal 32 channels, undersampling the spatial frequency of the electric field. Modern EEG systems now allow fast recordings of high density EEG with more than 100 channels.
Method Interictal epileptiform activity was recorded with 123 electrodes in 14 epileptic patients undergoing presurgical evaluation (5 hippocampal sclerosis, 7 neocortical lesions, 2 non-lesional). All patients became seizure free after operation. Each epileptiform potential was down sampled to 63 and 31 electrodes. A distributed source model (EPIFOCUS) was used to reconstruct the sources in the patient's individual brain with the three different electrode configurations. By calculating the distances from the inverse solution maximum of the individual spikes to the epileptogenic area, the localization accuracy with the three electrode set-ups was assessed.
Results Compared to 31 electrodes, 63 channels led to significantly smaller distances (i.e. better localization) in 9 patients and 123 electrodes to smaller distances in 11 patients. Over all patients the mean distance of the individual spike sources to the epileptogenic area was 16 mm for the 123 channel and 63 channel data and 30 mm for 31 channels.
Conclusion High spatial precision of epileptic source localization can be achieved with the EEG if the electric field is adequately sampled.

P 3043

Incidence of non-epileptic seizures in Georgian inpatient epilepsy population

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Background The incidence of non-epileptic seizures (NES) is significantly higher than clinicians realize. In a number of epidemiological studies conducted, it has been suggested that the incidence of NES is 5–20% and 10–40% in an outpatient and inpatient epilepsy population respectively (Gates J.R.).
Objective To assess the incidence of NES among the patients admitted to the neurological clinic with a preliminary diagnosis of epilepsy.
Methods 344 subjects (all female, aged 18–50, mean age 32.1±1.8) were investigated. All patients were admitted to the Epilepsy Center of Sarajishvili Institute of Neurology and Neurosurgery, Tbilisi, Georgia with a preliminary diagnosis of epilepsy. All subjects were monitored in the clinic over a 2–3 week period. MRI, CT and repeated EEG were performed for all subjects. Patients with pathology discovered by MRI or CT were excluded from the study. In 86 cases EEG-video monitoring was done.
Results For 258 (75%) patients diagnosis of epilepsy was confirmed. In 86 (25%) cases repeated EEG was negative and EEG–video monitoring was performed which revealed 54 (15.7%) cases of NES.
Conclusion The incidence of NES in the Georgian inpatient epilepsy population is comparable to the results of other similar studies (Sigurdardottir KR et all, 1998; Gates 1998). Our findings suggest that in all cases of epileptic seizures when repeated EEG is negative, EEG-video monitoring should be performed in order to exclude NES.

P 3044

Epilepsy in the elderly: A ten years clinical observation in 314 patients

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Objective To individuate in the elderly epilepsy the aetiology and frequent seizure types.
Materials We have analysed in a prospective study 314 epileptic patients 170 males and 144 females, admitted to our Neurologic Department in the last 10 years with epileptic seizures. All patients underwent clinical examination, routine blood laboratory tests, EEG, ECG, brain CT scan and, some of them, angiography and NMR.
Results The causes of epileptic seizures were: 1) acute cerebrovascular disease 110 pts; 2) brain tumour (glioma, meningioma, metastatic) 81 pts; 3) toxic-metabolic 60 pts; 4) dementia 21 pts; 5) head injury 15 pts; 6) marked cerebral atrophy 8 pts; 7) uraemia 4 pts; 8) CNS infection 4 pts; 8) multifactorial aetiology 8 pts; 9) sudden suspension of Lorazepan 3 pts.
Regarding the seizures types 136 pts had generalized tonic-clonic seizures (GTC), 140 simple partial seizures (SPS), 38 partial seizures with secondary generalisation. Regarding the aetiology of the seizures, all toxic-metabolic and due to sudden suspension of Lorazepan had GTC, whereas the majority of the pts. with cerebrovascular disease, brain tumour and head injury had SPS. In the other cases there was an equal distribution between GTC and SPS. Regarding the EEG, 143 pts. showed focal abnormalities, 88 widespread abnormalities and in 83 the EEG was normal. Brain CT scan and MRI was alterated in 221 pts. and normal in 93 pts.
Conclusions Epileptic seizures in elderly people are mostly due to focal brain lesions, which must be recognized with suitable, exhaustive investigations.

P 3045

The characteristics of patients with status epilepticus

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Status epilepticus (SE) is common and associated with significant mortality and complications. In this study, we investigated 348 consecutive SE incidents retrospectively to determine the characteristics of the patients, epilepsy, seizure, and SE classifications, etiologic factors for epilepsy and/or SE, therapy, outcome, and the factors affecting morbidity and mortality of SE.
The study group consisted of 273 patients (141 males, 132 females with a mean age of 36) with 348 SE incidents, who were admitted to the neurology clinics between 1989–2001.
The results showed secondarily generalized convulsive SE was the most frequent SE type with a percentage of 80.2. 72.1% of the patients had epilepsy before and over half of these patients (57.3%) had symptomatic partial epilepsy. AED discontinuation and systemic infection were the most frequent etiologic factors for SE in this group. Cerebrovascular accidents were the most frequent factor in the patients presenting with SE as the first seizure. Blood tests showed low level of glucose only in one patient, and 36% of the patients had high levels of glucose. Cranial CT and/or MRI results revealed infarction was the most frequent finding. SE was controlled with one medication in over half of the patients (51%), and only 4.4% needed to have

anaesthesia to control the seizures. Of all the patients 65.2% were discharged without any deficits, 27.3% had neurological deficits, and 7.5% of the patients had died.
Our results revealed old age, generalized convulsive SE, cerebrovascular disease, SE as the first seizure episode were factors rising morbidity and mortality.

P 3046

Levetiracetam in elderly patients with epilepsy

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Rational To evaluate the efficacy and tolerability of levetiracetam (LEV) add on therapy in elderly patients with epilepsy.
Methods Patients ≥50 years exposed to LEV in clinical development were analysed. Responder rates (≥50% and 75% seizure reduction) and seizure freedom were calculated and tolerability assessed.
Results 211 patients aged 50–78 years (median 56 years; 14.7% >65 years; median age at epilepsy onset 24.8 years) were included. Median LEV dose was 3000 mg/day, mean exposure 697 days. 43.6% of the patients took one other AED and 42.7% took two. 43.6% of patients were still receiving treatment at study period end. Treatment was terminated in 19.9% for adverse events (AEs), 15.6% insufficient efficacy, and in 11.8% for study completion. Median seizure reduction from baseline was 43.9% (vs. 39.6% total population) with a decrease of the median seizure frequency from 1.42/week at baseline to 0.84 during LEV. Seizure reductions of either ≥50% or ≥75% were comparable (37.2% vs. 38.6% and 18.6% vs. 20.1%, respectively). Seizure freedom during the 6 and 12 months prior to final evaluation was greater than in total population (19.0% vs. 11.7 % and 15.2% vs. 8.9%, respectively). AEs, mainly CNS-related and mild (e.g. somnolence, asthenia, dizziness), occurred with similar incidence to the total population without increase in effects expected higher in the elderly (e.g. confusion) and no idiosyncratic side effects.
Conclusions In elderly patients, LEV produces higher seizure freedom rates compared to the total population studied, with similar tolerability.

P 3047

Effect of levetiracetam on resistant photosensitivity

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Introduction Photosensitivity is not uncommon in people with uncontrolled primary generalised epilepsy, especially women, and may not respond to conventional anti epileptic treatment (valproate and/or lamotrigine). Levetiracetam (LEV) has previously been shown, in a single dose study, to have a sustained effect on photosensitivity. We report its effect on 20 patients with previously uncontrolled photosensitivity.
Method The notes of 20 patients with uncontrolled photosensitivity in the setting of primary generalised epilepsy and treated, in our department, with LEV were systematically reviewed: all patients had had full photoparoxysmal response assessments before, during and after treatment.
Results All patients treated had either photosensitivity, pattern sensitivity or both: all but one patient completely lost their photoparoxysmal responses: this beneficial result has been sustained on follow-up. 4 patients had eyelid myoclonia, which also responded.
Conclusion LEV appears to be effective in resistant photo and pattern sensitivity. A formal trial of its use in this area is clearly indicated.

P 3048

Effect of Levetiracetam on resistant juvenile myoclonic epilepsy

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Introduction Juvenile Myoclonic Epilepsy (JME) is a common syndrome of early morning myoclonic jerks, absences and tonic clonic seizures, usually treated by sodium valproate or lamotrigine. Not all patients fully respond however, and valproate is relatively contraindicated in women of childbearing potential. Levetiracetam (LEV) is closely related to piracetam, effective in resistant myoclonias, and therefore might be effective in resistant JME. We have been studying its use in this condition in an open study in our department.
Method The notes of 40 patients with resistant JME exposed to treatment with LEV in its usual dose escalation were reviewed for evidence of reduction in seizure frequency and drug-related side effects.
Results 60% of these patients became, and remained, totally seizure free and some have withdrawn from concomitant medication: only 8% had no effect at all. The drug (LEV) seems particularly effective in abolishing myoclonic jerks and concomitant photo or pattern sensitivity. A total daily dose of 4g seems useful in some patients: beneficial results do not fade with the passage of time.
Conclusion This is an impressive result in a group of patients resistant to conventional treatment and suggests that a formal trial of LEV in JME is urgently required.

P 3049

Postischemic stroke epilepsy in the elderly

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Rationale Cerebral ischemia and infarcts are the most frequent cause of epilepsy in the elderly. Seizures occurred in the first week after ischemia (early seizures) corresponds to acute symptomatic seizures, and the late seizures followed about one month after cerebral infarct are included in vascular epilepsy.
Methods This study was performed from January 1999 to January 2002. 139 patients with epileptic seizures and ischemic stroke were identified in our department. The patients were viewed depending on: age, moment of seizure onset, seizures type, recurrence, CT localization of ischemic stroke, atherothrombotic or embolic aetiology, EEG changes.
Results From 139 patients with postischemic stroke epilepsy, 57 presented early seizures (52 patients experienced seizures within 24 hours from the infarction), and 82 patients presented late seizures. Mean age was 67,8 years, 90 patients were men, 49 women. Seizures type were: 49 partial motor, 27 partial motor status, 40 partial motor secondary generalization seizures, 16 tonic-clonic status epilepticus, 7 partial sensitive seizure. The CT localizations of lesions were: 79 cortical, 35 subcortical and thalamic, 25 cortical and subcortical. 33 presented cardioembolic infarcts, 89 patients presented EEG changes, and 20 patients presented recurrent seizures.

Conclusions The incidence of poststroke epilepsy increases with age. The epilepsy risk for men after cerebral infarction is higher that for women. Cortical infarcts (frontal, parietal, occipital) are associated with higher risk for seizures than subcortical infarcts. Cardioembolic cerebral infarcts were risk factors for early seizures.

P 3050

The analysis of electroencephalographic patterns as a predictive factor on post-infarction seizures

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Background and objectives Post-infarction seizures are defined as an ictus that occur following a cerebral infarction in those without a prior seizure history. It is one of the most common causes of epilepsy, particularly in the elderly. There have been only few studies correlating electroencephalographic (EEG) findings to onset of post-infarction seizures. The aim of our study is to analyse EEG patterns that may help to identify those at risk for seizures after an infarction.
Methods Medical records were reviewed on 67 consecutive patients admitted to Pusan National University Hospital (PNUH) from September 2000 to January 2002, with diagnosis of cerebral infarction who had EEG within 2 days of stroke onset. Thirteen patients were identified who subsequently developed new epileptic seizure (post-infarction seizures). We compared EEG abnormalities of the patients with post-infarction seizure and those without seizures. Specific features of EEG patterns; amplitude, persistence, phase relations, morphology, and frequencies were analysed.
Results EEG presence of spike and sharp waves, PLEDs, 2 times high amplitude compare with contralateral lesion side, greater than 60% of abnormal delta wave index, steep ascending phase of slow wave, phase reversal of slow wave on the ipsilateral lesion side correlated with post-infarction seizure onset.
Conclusion This study suggests EEG is helpful in determining the risk for developing epilepsy after cerebral infarction. Risk analysis from baseline EEG shortly after an infarction can be helpful in optimal management.

P 3051

Autoimmune mechanisms in postseizure period in epileptic children

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Epilepsy in 75% of cases begins in childhood. Pathogenic mechanisms of epilepsy development require further analysis.
155 children (75 boys, 80 girls) aging from 3 to 15 were monitored. Along with neurological and EEG examination all patients were subjected to immunological examination in postseizure period. DNA-antibodies level was determined using immunoenzymatic method on first day after seizure and a month later. The control group included 20 children.
Anamnesis and neurological examination showed that in most cases epilepsy was caused by perinatal brain injury in form of hypoxic-ischemic and traumatic pathology of cerebrum. Seizure pattern in most cases was tonic-clonic and absentia epilepsy state. EEG examination showed epileptic activity in 43.9% and dysfunction of median brain structures in 56.1% cases. Immunological examination showed high anti-DNA level (0.607 ±0.02 ODU) compared to the control group (0.296±0.002 ODU). Anti-DNA level correlated with seizure frequency and epileptic activity in EEG data. Dynamic monitoring of anti-DNA level a month after the seizure showed its reliable ($p<0.005$) decrease compared to the first day; however it did not reach the normal value.
High anti-DNA level in post-seizure period and its dynamic decrease approved the presence of an autoimmune process whose intensity tends to diminish with time. Neuron's death leads to releasing of intracellular content and disintegrating of DNA. DNA ejection into extracellular space and its insufficient capture by astroglia causes neuron's death. Induction of specific and nonspecific brain barriers causes apoptosis and immune inflammation. Therefore, appropriate correction is required in post-seizure period in epileptic children.

P 3052

Molecular mechanisms of levetiracetam action on calcium channels in Ca1 hippocampal neurons

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Introduction Previously it was shown that antiepileptic drug levetiracetam (LEV) selectively depress the activity of high voltage activated calcium channels (HVA-CC) in CA1 hippocampal neurons. However the molecular principles of this inhibition are still unknown. Therefore, in the present experiments we studied these mechanisms.
Methods Whole-cell patch clamp and single channel recordings of HVA-CC activity of isolated hippocampal CA1 neurons of rat were performed. A two-pulse protocol was used to study voltage dependence of LEV action on steady-state inactivation, activation of HVA-CC and the time course of recovery from inactivation.
Results We established that in control conditions, the membrane potential at which half-inactivation occurred (V1/2) was –10.68mV and after 200μM LEV application it was –12.24mV. The slope factor (k) was 8.7mV and 7.73mV for control and LEV. Activation characteristics were V1/2=–6.8mV in control and –7.03mV after LEV application. The k was 9 mV for both cases. The amplitude of tail currents reflecting fraction of calcium channels remaining open at the end of test pulse was not changed by LEV. Usage of depolarising prepulse reversing the possible inhibition of HVA-CC by membrane-delimited action of G-proteins did not reverse the majority of LEV-induced inhibition.
Conclusions We concluded that LEV action slightly depends on extent of channel activation or inactivation and that LEV slightly influences HVA-CC kinetic characteristics. The mechanism of blocking LEV action is not connected with channel deactivation or G-protein pathways underlying LEV-inhibitory effect and presumably depends on direct action on channel molecule.
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P 3053

Piracetam (pyramem) in the treatment of cortical myoclonus

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Myoclonus is a rare, disabling symptom arising from a variety of pathologies affecting the nervous system. Involuntary movements can cause severe disability. Conventional treatment with

anticonvulsants such as sodium valproate, clonazepam and primidon often controls the seizures, but not the myoclonus jerks, despite optimum dosage.
The aim of the present study was to assess in an open trial therapeutic efficacy of Pyramem in patients with cortical myoclonus regardless of its underlying aetiology.
In 10 patients with myoclonic jerks from cortical origin Pyramem was given orally as add-on therapy to valproate and clonazepam. The initial dose of Pyramem was 7.2 g/day increasing every 3 days to maximum 19.2 g/day or until stable clinical benefit was evident. The median daily dose of Pyramem was 15.2 g. Efficacy was assessed using myoclonus rating score (Truong and Fahn, 1988).
A significant improvement with linear dose-effect relation in all patients was observed. Pyramem was well tolerated and essentially free of adverse effects, without drug interaction with the base-line anticonvulsive therapy

P 3054

Causes for drug therapy failure of idiopathic Epilepsies with mixed types of seizures

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Wrong choice of antiepileptic drug (AED) could be the reason for drug therapy failure of idiopathic epilepsies with mixed type of seizures. The aim of our study was to remind and to support this possibility. A total of 28 patients were hospitalised due to refractory of their seizures. The patients were between 12 and 46 years old (20.92±4.54), the onset of the seizures ranged between 5 to 26 years of age (13.25±3.64), while the time duration of the disease was 2 to 25 years (8.89±2.98). The patients were on continuous treatment with carbamazepine, phenobarbiton, phenytoin and primidon, as mono- or polytherapy from the seizure onset until the moment of their hospitalisation.
Careful investigations allowed to revise the diagnosis on the following way: 15 patients suffered from juvenile myoclonus epilepsy (JME), 11 patients from grand mal on waking, 1 from juvenile absence epilepsy (JAE), and 1 patient from phantom absences and grand mal. Previous therapy in all of them was replaced with monotherapy of valproate. At least one year complete control of GTCS was achieved in all patients with JME, in 9 of 11 patients with grand mal on waking and in the other 2 patients.
Carbamazepine, phenobarbiton, phenytoin and primidon appeared to be ineffective AED in our group of patients with mixed types of seizures. Contrary, valproate showed more satisfactory effect.

P 3055

Effect of antiepileptic drug monotherapy on crystalluria in children and young adults

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Introduction Urolithiasis is a rare side effect of antiepileptic drugs (AEDs) in children and young adults. Because crystalluria is frequently associated with urolithiasis, the relationship between AEDs and crystalluria was investigated for the first time.
Methods Urinalysis was retrospectively studied in epilepsy patients treated with AED monotherapy for more than one month. A total of 886 urinary specimens were enrolled from AED-taking patients aged from five months to 28 years. They were compared with urine samples from 780 age-matched controls and 112 patients before starting AEDs. AEDs administered in this study were: carbamazepine, valproate, phenobarbital, zonisamide (ZNS), sulthiame (STM) and phenytoin.
Results The frequency of crystalluria was higher in patients treated with ZNS ($p<0.0001$) or STM ($p<0.05$) than that in controls, other AEDs and patients before starting AEDs. The age was higher in controls with crystalluria than that in controls without crystalluria ($p<0.001$). There was no such age difference in patients treated with ZNS or STM. The blood concentration of STM was higher in patients with crystalluria than that without crystalluria ($p<0.05$). There was no such difference in ZNS-taking patients. Male patients on ZNS therapy were more likely to have crystalluria than female patients ($p<0.001$). There was no such sex difference in patients on STM therapy.
Conclusions Patients treated with ZNS or STM are likely to have urolithiasis. Male patients on ZNS therapy and high blood concentration of STM are risk factors for urolithiasis.

P 3056

Levetiracetam in combination with other antiepileptic drugs shows enhanced antiepileptic activity in animal models

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Introduction While monotherapy remains the treatment of choice for epilepsy, seizure control is not always achieved and rational polypharmacy is undertaken. The combined action of different antiepileptic drugs (AEDs) is an important subject, not only in reference to seizure control, but also in the context of obviating adverse events. This study utilized a preclinical paradigm to investigate the anticonvulsant effects, pharmacokinetic profile and CNS adverse effects associated with combination therapy using levetiracetam (LEV) and some of the more classical AEDs.
Methods Genetically sound-sensitive male mice (n=10/group) were assessed for protective ED_{50} determinations of classical AEDs, valproate (VPA), clonazepam (CZP), phenobarbital (PB), carbamazepine (CBZ), and phenytoin (PHT) and for LEV. LEV (fixed dose of 5.5 mg/kg) was combined with the other AEDs and a dose-response curve of protection against clonic convulsions was calculated. Doses inducing CNS adverse effects (TD_{50}) were determined by rotarod impairment and compared with combination therapy. Plasma and brain AED levels were determined by GC/MS, GC/EC, HPLC/UV and FPIA analysis.
Results Co-administration of LEV with VPA, CZP, PB, CBZ and PHT enhanced anticonvulsant potency, resulting in 28-, 23-, 16-, and 2-fold increases, respectively. Conversely, there was no enhancement of the CNS adverse effects. The plasma and brain levels of LEV and the other AEDs were not modified during co-administration.
Discussion The results of this study suggest that co-administration of LEV with VPA, CZP and PB markedly enhances anticonvulsant potency while not increasing CNS adverse effects, suggesting a synergistic pharmacodynamic effect.

P 3057

Pilocarpine-induced status epilepticus: effects of chronic treatment with levetiracetam and valproate

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Introduction Status epilepticus (SE) is a neurological emergency and associated with a high morbidity/mortality rate. The aim of this study was to induce epileptogenesis in rats by administration of pilocarpine (PILO; ip) and to compare the anti-epileptogenic effects of levetiracetam (LEV) and valproate (VPA).
Methods Male Sprague-Dawley rats were administered PILO (375 mg/kg, ip) and SE terminated after 30 min with diazepam (10 mg/kg; iv). Separate groups were administered either LEV (54 mg/kg; ip) followed by 21 days LEV infusion (50, 150, or 300 mg/kg/d) or VPA (200 mg/kg; ip), followed by 21 days VPA infusion (600 mg/kg/d). The incidence of spontaneous seizure, evoked field potentials (DG and CA1 hippocampal areas), and hippocampal histopathology were examined 3 days after termination of the chronic infusion.
Results The incidence of spontaneous seizures did not differ between groups. LEV treatment dose-dependently reduced the increase in population spike (PS) amplitude in the DG area; while VPA treatment reduced, not significantly, the PS amplitude. Paired-pulse inhibition in the hippocampal CA1 was eliminated in PILO-treated rats, but restored by LEV, but not VPA, treatment. LEV treatment (150, 300 mg/kg/d) reduced, not significantly, the PILO-induced hippocampal necroses; no difference was observed in the VPA-treated animals.
Conclusion LEV treatment (150, 300 mg/kg/d) reduced the epileptogenic effect induced by PILO, as 1) a reduction in amplitude of the PSs, 2) a restoration of paired-pulse inhibition and 3) a modest decrease in neuropathological consequences. VPA (600 mg/kg/d) did not reveal any significant effects on these parameters.

P 3058

Levetiracetam has no measurable binding to, or observed antagonist effect at, metabotropic glutamate receptors

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Introduction Levetiracetam (LEV) is an antiepileptic drug utilized as adjunctive therapy for partial seizures in adults. Because the exact molecular mechanism of action of LEV is currently unclear, we tested whether LEV might act by modulating metabotropic glutamate receptors (mGluRs). Several mGluR family members have been linked to seizure activity, making this family of receptors attractive as potential sites of LEV action.
Methods We utilized 3H-LEV as a probe to examine the binding of several mGluR ligands at a brain-specific binding site for LEV. To further test this compound, in vivo experiments evaluated the ability of LEV to counteract behavioural changes induced in mice by intracerebroventricular infusion of 1S,3R-ACPD (200 nmol/min).
Results Neither glutamic acid nor any of the subtype specific mGluR ligands (S)-AP-4, quisqualic acid, and (2S, 3S, 4S)-CCG, displaced 3H-LEV in crude rat brain membranes. However, there was a minor displacement observed with the non-specific mGluR agonist 1S,3R-ACPD. In contrast, LEV (5.4–170 mg/kg; i.p. –60 min) did not significantly prevent the face washing and hind limb scratching induced by 1S,3R-ACPD.
Conclusions Various ligands known to interact with mGluRs did not displace 3H-LEV in crude rat brain membranes. While LEV did cause a modest displacement of the non-specific mGluR agonist, 1S,3R-ACPD, there was no change in the glutamate agonist-induced behaviour. These results suggest that the antiepileptic mechanism of LEV appears to be unrelated to a modulation of mGluRs.

P 3059

Levetiracetam does not alter body weight: analysis of randomised, controlled clinical trials.

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Introduction Body weight increase is a clinically significant adverse effect of several antiepileptic drugs (AED) including valproate and gabapentin. The objective of this evaluation was to examine the effects of LEV treatment on weight.
Methods We reviewed data from 4 prospective, placebo (PBO)-controlled, clinical trials. The analysis included men and women, >16 years old, who had LEV exposure for ≥1 month. Body weight was measured at baseline and final LEV study visit. Data was analysed by gender, body mass index (BMI), duration of LEV exposure and concomitant AED treatment. Data presented is mean values (SD).
Results Analysis included 970 patients (mean 37.5 years, 54% men/46% women); LEV (n=631) PBO (n=339). Mean LEV dose was 2053mg/d (maximum 4000mg/d) and duration was 125 days (max=181 days). Concomitant AED therapy included CBZ=647, GBP=92, LTG=89, PHT=207, VPA=196, PB=77, VGB=75 patients.
Mean body weight at baseline vs final study visit at 1–3 months and >3 months for LEV patients was 74.3 (16.6), 76.6 (17.5) and 75.8 (16.8) kg, respectively (NS). For PBO, 72.4 (15.5), 74.0 (16.8) and 74.6 (16.9) kg (NS). Clinically significant weight change, defined as >7% change from baseline, occurred in 8.8% of LEV patients (4.4% increase/4.4% decrease) vs 9.4% (5.9% increase/3.5% decrease) in PBO. Subgroup analysis revealed that only male patients receiving PBO had modest, yet statistically significant weight change (+0.8–1.0 kg in n=148 with BMI=19–30, $p<0.003$).
Conclusions We conclude that treatment with LEV was not associated with weight change during controlled clinical trials. LEV appears to be a weight neutral AED.

P 3060

Dose-response relationship of Levetiracetam

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Objective To evaluate the dose-response relationship (efficacy and tolerability) of levetiracetam (LEV) as adjunctive therapy in adult patients with partial epilepsy.
Methods Pooled data from double-blind, randomised, placebo-controlled trials (n=904) were used to assess the efficacy of LEV at doses of 1000–3000mg/day. Both periods of a cross-over study were analysed and a within-patient (n=93) cross over analysis, comparing LEV 1000 mg and 2000mg, conducted. Tolerability to LEV was also assessed in these trials, including

both cross-over periods, and an additional safety study (n=119), a total of 1023 patients.
Results A dose-response relationship was observed with LEV for ≥50% responder rates; increasing from 29% at 1000 mg, 34% at 2000 mg and 41% at 3000 mg. Within patient analysis for 1000 mg and 2000 mg/day LEV showed 2000 mg to increase responder rate by 33–70% and odds of obtaining response by 4.2 compared to 1000 mg (98% CI: 1.0, 17.2). Seizure freedom (the ultimate aim of treatment) also showed a dose-response to LEV; 4.7%, 6.3% and 8.6% at 1000 mg, 2000 mg and 3000 mg doses respectively. There was no evidence for a dose-related adverse effects relationship (asthenia, dizziness and somnolence) at doses of 1000 mg to 3000 mg. At 4000 mg doses, somnolence occurred more frequently. However this group consisted of only 38 patients who started immediately on LEV 4000 mg without dose titration.
Conclusion LEV was effective and well tolerated decreasing seizure frequency in a dose-dependent manner with 3000 mg/day providing the greatest seizure freedom.

P 3061

Interactions of lamotrigine with some antiepileptic drugs – an isobolographic analysis

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The isobolographic analysis distinguishes 3 most important types of interactions, among them the most accepted are: pure additivity, supra-additivity and sub-additivity.
The present study was aimed at determining the exact type of interactions between lamotrigine (LTG) and diphenylhydantoin, carbamazepine, valproate, phenobarbital and topiramate in the maximal electroshock seizure (MES) test in mice. The activity of two-drug mixture, applied in 3 fixed dose ratio combinations, was estimated and expressed as the ED_{50} values (dose protecting 50% of animals) of these drugs against MES-induced seizures in mice. Moreover, the adverse effects were determined in the chimney test and passive avoidance task in mice.
Interactions between LTG and topiramate or phenobarbital caused a supra-additive interaction as regards their therapeutic activity in the MES test. Simultaneously, the interaction of LTG and topiramate demonstrated a sub-additivity in respect to evoked side effects in the chimney test, whilst the interaction of LTG and phenobarbital in this respect, was supra-additive. Isobolographic analysis revealed the antagonistic interaction between LTG and carbamazepine in the MES test. In contrast, interactions between LTG and diphenylhydantoin or valproate showed a pure additivity, in both MES and chimney tests. Moreover, all combinations of LTG with studied antiepileptics induced no adverse effects, evaluated in the passive avoidance task.
Finally, the isobolographic analysis revealed that LTG combined with topiramate, diphenylhydantoin or valproate generally might result in positive (additive or supra-additive) interactions, in the clinical practice.
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P 3062

Epileptic seizures in children with cerebral paralysis

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Introduction Cerebral paralysis is usually defined as non-progressive disorder with motor disturbances caused by the lesion of the immature brain, which is also a reason of increased excitability and decreased inhibition responsible for the seizures.
Objectives Establish the frequency of the seizures in children suffering from cerebral paralysis and the age at which the attacks are most frequent.
– Most common form of seizures.
– The possibility of controlling the attacks with conventional and new antiepileptics.
Methods A group of 34 patients under 13 years old was analysed (19 males and 15 females) treated in the Krusevac Hospital under the diagnosis of CP in the period of five years.
Results Seizures are recorded in 16 cases (46.5%). In 12/16 patients (75%) the attacks started in the first two years of their life. In 2/16 (12.5%) patients the first seizure happened after the age of 10.
Based on the EEG results we established that the most common type of seizures are partial or secondary generalised seizures.
Epileptiform EEG changes were registered also with children who don't have epilepsy.
Control of the seizures with conventional and new antiepileptics was accomplished in 10/16 (62.5%) patients and incomplete control in 6 patients (37.5%) – with monotherapy in 6/16 (31.24%) and polytherapy in 10/16 (68.76%) patients.

P 3063

Serum thyroid hormones concentrations in post-menopausal women with epilepsy

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Purpose The aim of the study was to evaluate the serum T4, FT4, T3, FT3 and TSH concentrations in postmenopausal epileptic women.
Material and methods 20 postmenopausal women aged 51–65 treated because of epilepsy for 5–49 years were studied. The seizure frequency amounted to several seizures per month and several per year. Fifteen patients received CBZ (3 of them with PHT) and 8 women were treated with PHT (3 of them with CBZ). The control group consisted of 20 healthy women. In all women serum concentrations of T4, FT4, T3, FT3 and TSH were performed by RIA taking blood samples at 8.00.
Results Mean serum T4, FT4, FT3 and TSH concentrations in postmenopausal women with epilepsy were significantly decreased and mean serum T3 concentration was significantly increased as compared with the control group. There were no significant correlations between mean serum hormone concentrations and the aetiology of epilepsy, the seizure type, the seizure frequency and the treatment applied. None of the patients developed symptoms of hypothyroidism.
Conclusions In our patients inducers of the liver microsomal enzymes probably caused an increased metabolism of thyroid hormones – T4, FT4 and FT3. There is also a possibility of decreased hormones synthesis in the thyroid gland. Signifi-

cantly increased serum T3 concentration suggests that CBZ and PHT increase the conversion of T4 to T3. The decreased serum TSH concentration may suggest that the feedback system is not activated.

P 3064

Subacute encephalopathy with seizures in alcoholism (SESA); more common than described?

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SESA syndrome is a very rarely reported dramatic complication of chronic alcoholism first described by Niedermeyer in 1981.
We are presenting cases of three chronic alcohol abusers who developed recurrent seizures and prolonged encephalopathy. Focal neurologic signs were found on examination. The results of neuroimaging and CSF investigations were unremarkable. The EEG changes were, however, severe, with periodic polyspikes evolving to PLEDs, focal slowing and gradually improving. Two patients developed pneumonia through the course of the disease. All patients eventually recovered.
SESA syndrome consists of prolonged encephalopathy, focal or generalised seizures, focal neurologic signs and prominent focal EEG changes without gross structural lesions. Patients often develop internal medical complications and usually recover.
With our cases we would like to remind clinicians about this severe complication of chronic alcoholism, with relatively good prognosis. According to our observations the SESA syndrome is more common than described.

P 3065

Juvenile myoclonic epilepsy in the elderly

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Juvenile Myoclonic Epilepsy (JME) is an idiopathic generalized epileptic syndrome that has only recently attracted considerable attention. Remarkably, JME is often diagnosed with delay because of physicians involved, including the specialists, are not familiar with a disease whose nature has yet to unfold. JME is believed to be a lifelong epilepsy. However, this view has been debated from time to time. In a total of 37 patients with JME (mean age: 22.5 years) attending our epilepsy out-patients' clinic at the 1st University Department of Neurology, we present two cases where definitive diagnosis of JME was delayed until the age of 60 and 65. The two patients, a male and a female, fulfilled the diagnostic criteria for JME. They presented refractory seizures (myoclonic jerks and tonic-clonic) and were treated with carbamazepine, vigabatrin, phenobarbital, phenytoin and gabapentin. MRA demonstrated multiple gliotic lesions. We conclude that the small percentage of elderly patients with JME in our group of patients with JME suggests that JME is not a lifelong epilepsy. The two cases may represent two non-diagnosed cases in which the delay in diagnosis and the non-appropriate treatment provoked secondary lesions in the brain, which conserved the epilepsy.

P 3066

The role of inherent tendency to febrile seizures

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Objective Recent investigations [1, 2] support the opinion that epilepsy is either an inherent disease or has a genetic tendency. It was found out a tendency to seizure reactions on hyperthermia with age-dependent penetration.
Methods To research the role of inherent factors for appearing of febrile seizures and to define genetic interrelations between febrile seizures and epilepsy we investigated a family history of 33 children with unique episode of febrile seizures and 26 children with recurrent febrile seizures. Age of the children was from 4 to 6 years. EEG was performed for all the children and their relatives.
Results Examination of relatives of the children with febrile seizures demonstrated that 14% of parents, 25% of sibs, 7% of aunts and uncles, 10% of cousins had the same seizures. Incidence of epilepsy among relatives was 10%. Different conditions suggested by many authors as epi-equivalents (headache, enuresis, etc.) occurred in 33% of cases.
Conclusion The febrile seizures appear and repeat with a lower body temperature including a subfebrile one if inherent burdening of epilepsy and/or febrile seizures occurs both in paternal and maternal lines.
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P 3067

Epileptic seizures related to ischemic stroke

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Cerebral ischemias are the largest group of strokes and the most frequent cause of epileptic seizures and vascular epilepsy.
Purpose To study risk factors, clinical polymorphism and morphology of seizures occurred in patients with cerebral ischemic stroke, to find correlations between clinical, biochemical, electrophysiological and neuroimaging findings.
Methods We examined 1162 patients with ischemic stroke hospitalised in Clinic of Neurology of Emergency City Hospital during 1997–2001. 58 of them developed epileptic seizures and underwent: clinical examination, laboratory tests determining fat metabolism and inflammatory markers, EEG, EEG mapping, and cerebral CT or MRI investigations.
Results In our study 58 (4.99%) patients, 34 (58.6%) male and 24 (41.4%) female, with mean age of 58–98 years, developed vascular epileptic seizures. 25 patients (43%) have early seizures, and 33 (57%) late seizures. The morphology of fits was following: 4 cases – generalized absence seizures, 3 cases – status epilepticus, and 51 (87.9%) – partial secondary generalized seizures. In about 60% total cholesterol, LDL cholesterol and beta-lipoproteins were elevated. The localization of focal component was alike that of cerebral infarction. In 70% of patients specific paroxysmal EEG changes were observed. Cerebral CT and MRI revealed ischemic foci with cortical and subcortical involvement.

Conclusion Morphology of post-stroke seizures in majority of cases was represented by partial secondary generalized seizures; localization of focal component was similar with localization of cerebral infarction, CT and MRI revealed cortical involvement. An elevation of total cholesterol and its derivatives is observed in most of the patients.

P 3068

Onset determining factors for post-traumatic epilepsy

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Head traumas (HT) accounts approximately 30–40% of all traumas and represents the major cause of disability in young adults. Post-traumatic epilepsy (PE) is one of the most severe consequences of HT. Occurring in early period of HT post-traumatic seizures are often ignored and not treated specifically in time.

The **aim** of the study was evaluation of risk factors for post-traumatic epilepsy.

Materials and Methods Our study was performed in a group of 84 patients with PE, 58 of whom were males and 28 females. Studied patients were in the age ranges: 20–30 years – 17 persons; 31–40 years – 25 persons; 51–60 years – 10 persons. Patients' personal history was collected in order to evaluate precipitating factors as following: febrile seizures in childhood, enuresis, sleepwalking, family or personal history of inherited epilepsy or psychic disorder, episodic loss of consciousness. The three most important HT forms were: in 37.5% – concussion, in 57.5% – cerebral contusion, and in 5% – opened cranial cerebral trauma. Epileptic seizures occurred at different time periods after HT. Thus the PE incidence is about 17% during first 3 months after HT, 28.5% – during further 3–12 months and 55.5% – after one year following HT.

Results Our study revealed that PE was caused by following factors: cerebral contusion, opened craniocerebral trauma, recurrent HT, loss of consciousness, early post-traumatic seizures.

Conclusions Evaluation of risk factors for PE makes possible early diagnosis of PE, initiation of early specific treatment and prevention of severe disability caused by epilepsy.

P 3069

Does familiarity affect attitude and practice toward epilepsy?

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Social acceptance of epilepsy is a burden for patients and their relatives. The awareness, understanding and attitudes towards epilepsy were evaluated in a pilot study with 250 persons. The survey consisted of 10 questions and was conducted by one-to-one interview. Regarding all subjects 81% had heard about epilepsy; 73% had no objections to social association; 66% believed that epileptics should be employed in equal jobs. Older age and less education showed a non-significant trend to negative attitude. This population has been divided into two strata: those who know someone with epilepsy (FWE) and those who do not (NFWE). Prejudice toward the disease did not differ between groups; 71% of NFWE and 73% of FWE did not object to their children associating with epileptic ones; 70% of NFWE and 67% of FWE objected to their children marrying an epileptic person; 57% of NFWE and 53 % of FWE believed that epileptic persons should be employed in jobs like other persons; 36% of NFWE and 13% of FWE group had no opinion about the cause of epilepsy; 28% of NFWE and 6% of FWE responded that they did not know how to help a person having seizure. Knowledge and practice were not different between groups. Familiarity did not improve the attitude toward disease as would be expected. Community health education should attempt to concentrate on first aid measures.

P 3070

Myths and ideas concerning epilepsy among relatives of Portuguese epileptic patients

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Introduction The SPOKE trial showed that Portugal ranks second among countries with the least informed population as far as epilepsy is concerned.

We wanted to know if the relatives of epileptic patients attending our consultation had accurate notions regarding the disease, compared to those of the general population.

Methods We applied a questionnaire to 101 individuals – 45 relatives – R; 56 non-relatives – NR. Statistical analysis used non-parametric tests of *Qui-quadrate* and exact test of Fisher.

Results 84% said epilepsy was a neurological disease (100% of R, 71.4% of NR); 13% a psychiatric disease (23.2% of NR); 1% an infectious disease (1.8% of NR); 2% of another aetiology (3.6% of NR). 81% identified a connection between alcohol, stress and epilepsy (91% of R, 73% of NR). 58% denied connection with mental retardation (47% of R, 68% of NR). 76% admitted hereditary factors (84% of R, 70% of NR). 84% said epileptic patients could have normal lives (87% of R, 82% of NR) and regarding work, family and treatment the answers were similar in both groups. 80% had witnessed a seizure (93% of R, 70% of NR). Regarding what to do during a seizure: R chose removing sharp objects and calling the emergency number (EN); NR chose calling EN and placing an object inside the patients' mouth.

Conclusions Relatives showed good knowledge of the disease, although in general questions the results were similar in both groups. In specific questions and practical issues, the answers were significantly better among relatives.

P 3071

Law regulations, driving ability of patients with epilepsy and traffic safety

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Our Law has draconian regulations: a person having got one single epileptic seizure is forbidden to drive, and the doctors are obliged to report their patients having seizures. The aim of this study was to see how much this law regulation has been respected by the patients and by the doctors.

We have interviewed 99 patients with epilepsy with seizure experience between 3 to 33 year-old (9.85±3.1) for respectability of law regulations. Seventy-five (75.75%) patients did not respect the legal prohibition; 11 of these 75 patients acquired driving licence after the disease onset, the other patients had their driving licence prior to seizure onset.

All patients interviewed had regular antiepileptic therapy. Thirty-three (44%) of these 75 patients did not reach a two-year interval without seizures. Majority of them drove private cars, but nine of them were professional drivers of cars. Nine (12%) of these 75 patients with poor seizures control were participants

in traffic accidents (8 with material damage, and one died, the last one was a doctor). The doctors did not obey their duty to report their patients, but they always informed the patients for the character of the disease and the duties arising from the Law.
It becomes clear that more strict law has not been obeyed by anyone and makes the situation which endangers the lives of the patients as well as the lives of other traffic participants. From here arises the need for its essential change and introduction of more liberal solutions.

P 3072

Prefrontal "cortex" and system of antiepileptic defence: experimental and clinical – neurophysiological investigations.

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P 3073

Cancelled

P 3074

Adjunct anti-primary generalised seizure adjunct therapy for 39 case of refractory PGE (Primary generalised epilepsy)

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P 3075

Primary generalized epileptic seizures and Föhn in Bielsko-Biala

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P 3076

Fuzzy logic based on clinical evaluation of patients with complex partial epilepsy; Case Studies

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P 3077

Fluctuating isolated memory impairment; an unusual case of temporal epilepsy

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P 3078

Our experiences in the use of MRS in children with different types of epilepsy

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Headache and pain 2

P 3079

Systemic nitroglycerine decreases CGRP-afferents to rat caudal spinal trigeminal nucleus, an effect modulated by estrogen

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Introduction Systemic administration of nitroglycerine, a nitric oxide (NO) donor, triggers in migraine patients, but not in healthy volunteers, a delayed attack of which the mechanisms are unknown. Migraine is after puberty by far more prevalent in women and attacks can be triggered by abrupt falls in plasma estrogen levels, which accounts in part for sexual dimorphism, but lacks an established neurobiological explanation.
Method We studied therefore the effect of subcutaneous nitroglycerine (10 mg/kg) on the innervated area of calcitonin gene-related peptide (CGRP) containing afferents to the superficial laminae of the spinal portion of trigeminal nucleus caudalis (sTNC) and its modulation by estrogen.
Results In male rats, nitroglycerine produced after 4 hours a significant decrease of the area innervated by CGRP-immunoreactive afferents. These effects were not observed in the superficial laminae of thoracic dorsal horns. The effect of nitroglycerine was similar in ovariectomized females (ovx). In estradiol-treated ovariectomized females (ovx+E2) the area in laminae I-II of sTNC covered by CGRP-immunoreactive fibers was lower and not significantly changed after nitroglycerine. The bouton size of CGRP profiles was smaller in ovx+E2 animals; after nitroglycerine it decreased significantly only in males and ovx rats.
Conclusion NO donor nitroglycerine, is thus able to differentially influence CGRP containing fiber populations in the superficial laminae of the rats' TNC. Estradiol modulates the basal expression of this transmitter and blocks the nitroglycerine effect. These data may contribute to a better understanding of the cellular mechanisms by which estrogen can influence migraine severity and the triggering of attacks by NO.

P 3080

Nitroglycerine induces long-lasting hyperalgesia in rats – a neuropharmacological study

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Introduction Nitric oxide is a gaseous substance that plays an important role in nociceptive transmission and central sensitisation. Nitroglycerine is a nitric oxide donor whose effects on the central nervous system have been extensively investigated in recent years. Neuro-physiological and neuropharmacological studies have demonstrated that derived-derived nitric oxide evokes biological effects on neuronal activity in rat brain.
Method In the present study, we sought to evaluate the effects of nitroglycerine, on the behavioural nociceptive responses induced in rats by the formalin test, a well-known test of tonic pain based on the injection of algogenic agents intradermally, at different times from the drug administration. The possible role of cyclo-oxygenase (COX) activity and NMDA receptors was investigated by means of neuropharmacological probes.
Results Following systemic nitroglycerine administration, an increase was observable in the number of flinches during phase II of formalin test, from 1 to 4 hours post-injection. 4 hours after the injection of nitroglycerine, a significant increase was also observed in phase I of formalin test. Pre-treatment with indomethacin, a COX inhibitor significantly reduced the number of flinches in both phases of the text. MK-801, a non-competitive NMDA receptor antagonist, blocked nitroglycerine-induced nociceptive behaviour in a dose-dependent manner.
Conclusion These findings suggest that systemic nitroglycerine induces a long lasting hyperalgesic state that is mediated by cyclo-oxygenase and glutamate-dependent mechanisms.

P 3081

Patients with migraine prefer zolmitriptan orally disintegrating tablets over conventional sumatriptan tablets and rizatriptan orally disintegrating tablets

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Introduction Zolmitriptan orally disintegrating tablet (ODT) enables patients to treat migraine quickly, conveniently and discreetly when water is not readily available, and is useful for patients with migraine who have nausea or difficulty swallowing conventional tablets.
Method In an international survey, when migraineurs were asked which formulations of migraine medication they would prefer.
Results The most popular choice was a tablet that dissolves in the mouth and can be taken without liquids. Preference data from patients treated with zolmitriptan ODT indicated that the majority of patients felt the ODT could be taken sooner (70%) and was more convenient to take (78%) than conventional tablets, and liked the orange taste of the ODT (80%). This was confirmed in a crossover study, in which patients treated their migraine attacks with zolmitriptan ODT 2.5mg and with sumatriptan conventional tablet 50mg. A significantly greater proportion of patients preferred zolmitriptan ODT overall (60.1% vs. 39.9%; p=0.0130), and for convenience and ease of use, compared with sumatriptan tablet. Similar preferences were seen among patients with nausea or vomiting at baseline, or with difficulty swallowing tablets. Another comparative study (in migraineurs during a migraine-free period) found that migraineurs strongly and significantly favoured zolmitriptan ODT over the rizatriptan wafer (70% vs. 27%; p<0.001), in terms of taste and convenience. Preference for individual features of the taste and packaging also significantly favoured zolmitriptan ODT over rizatriptan wafer.
Conclusion These studies show that zolmitriptan ODT is the preferred formulation for migraineurs compared with both conventional sumatriptan tablets and the rizatriptan ODT.

P 3082

Benign thunderclap headache – retrospective evaluation of 71 patients admitted to our Neurological Dept between 1990 – 2002.

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Introduction Thunderclap headache (THC) is a descriptive term of sudden and hyperacute headache most often occurring for the first time in life. It may represent a serious underlying disease such as subarachnoid haemorrhage, unuttered aneurysm but can also occur in the absence of pathologic conditions.
Method The aim of this retrospective study was to evaluate the incidence of idiopathic and symptomatic thunderclap headaches in patients admitted to the Department of Neurology. We also focused on and analysed idiopathic THC regarding to it syndromes, course and concomitant diseases.
Results The diagnosis of idiopathic THC was established in 71 of 368 patients presented to the Neurological Dept. between 1990–2002 with thunderclap headache. Most patients with idiopathic THC complained of "thunder-like" headache with mainly occipital localisation. No history of similar headaches or positive family history was noticed. Neurological examina-tion revealed transient focal symptoms in 20% of patients, 42% presented with nausea or vomiting, 18% had neck stiffness. The most common concomitant diseases were acute or chronic infections and hypertension. 40% of patients had elevated inflammatory markers which normalised during hospitalisation in 20% of cases. We observed seasonal incidence with the highest incidence in summer and winter.
Conclusion 20% of patients presented to the Neurological Dept. with THC consist of idiopathic, benign condition of unknown aetiology. Observed seasonal incidence with coexisting signs of infection in 40% of patients may suggest the role of inflammatory process in benign THC pathogenesis.

P 3083

Triptan tablet consumption per attack (24 hours) in Spain: survey extension to include almotriptan

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Introduction The objective of our study was to compare patient self-reported tablet consumption of rizatriptan 10mg per attack with that of almotriptan 12.5mg in migraine patients in a pharmacy setting and to combine these data with a previous triptan survey.

Method Patients attending a pharmacy for a triptan prescription recorded the baseline pain intensity, the number of tablets of triptan per attack and 2 hour satisfaction. Univariate comparisons: ANOVA or Student t Test and Chi-square or Fisher exact test. A generalised estimating equation method was used to correct for within-subject correlation. Adjusted OR [95% CI] confidence intervals were calculated.
Results A previous survey showed that rizatriptan tablet consumption (mean±SD; 1.24±0.56) was lower than for sumatriptan (1.75±1.2, $p<0.05$); zolmitriptan (1.61±0.86, $p<0.05$) and naratriptan (1.46±0.62, $p=0.05$). In this survey, 118 patients were recruited and yielded 297 evaluable migraine attacks (rizatriptan=118; almotriptan=97; nontriptan=82). Rizatriptan consumption (1.22±0.49) was significantly lower than for almotriptan (1.55±0.65, $p<0.001$). The proportion of attacks treated with one triptan tablet was higher for rizatriptan (80.4%) than for almotriptan (53.6%, $p=0.001$). Almotriptan treated attacks had a more than three times greater likelihood of taking a second dose than rizatriptan (AdjOR 3.42 [95% CI 1.75–6.69], $p=0.008$). Patients were significantly more (27%) satisfied at 2 hours with rizatriptan (88.3%) than with almotriptan (69.2%) (AdjOR 3.32 [95% CI, 1.38–8.08], $p=0.008$).
Conclusion Triptan tablet consumption and likelihood of using more than one tablet per attack was significantly lower with rizatriptan than with other triptans. Patients were significantly more satisfied at 2 hours with rizatriptan than with almotriptan.
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P 3084

Familial occurrence of migraine with aura in a population-based study

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Introduction To better define a possible genetic basis for migraine with aura (MA), we investigated its familial occurrence in a sample of MA patients (17 women and 9 men) recruited from an epidemiological study of MA among the general population.
Method The patients were selected out of a total of 1,392 subjects (842 women and 550 men) representative of the general population aged 18 to 65 years in the southern Italian town of San Severo. MA family history was determined through direct interviews with all living first-degree relatives of the 26 MA patients who could be reached by investigators, i.e. 119 people (71 women and 48 men). MA diagnosis was made according to the 1988 International Headache Society (IHS) criteria.
Results Of our 26 MA patients, 7 (6 women and 1 man) had a family history of MA, with a total of 7 first-degree relatives affected by the disease (1 mother, 2 fathers, 1 brother, 1 sister and 2 children). Based on the MA lifetime prevalence rate (1.6%) in the San Severo general population, the relative risk (RR) of MA in the first-degree relatives of our patients was 3.68, i.e. 4.16 for females and 2.77 for males.
Conclusion Our RR rate was very close to that of Russell (3.79 in 1995), but markedly lower than that of Kalfakis et al. (11.8 in 1996). Though comparable to Russell's, our RR rate was estimated from substantially different MA lifetime prevalence rates, both for the general population and for relatives of MA patients.

P 3085

Mood disorders in migraine with aura subjects: an epidemiological study on the general population

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Introduction In our epidemiological study of migraine with aura (MA) among the general population of the southern Italian town of San Severo, we investigated the presence of mood and anxiety disorders in a sample of 26 patients (17 women and 9 men) with MA.
Method The patients were recruited from a representative sample (1392 subjects aged 18 to 65 years) of the San Severo general population. As controls we recruited 52 non-MA subjects sex- and age-matched (±2 years) to our MA patients. Both cases and controls were tested with the Italian-language M.I.N.I. 4.4 version of the SCID structured interview based on the 1994 diagnostic criteria for DSM-IV, in order to determine the presence of mood and anxiety disorders.
Results Comparison between data from the interviews with MA patients and controls showed: 1) episodes of major depression and dysthymia in 26.9% of MA patients versus 25.0% of controls; 2) manic and/or hypomanic episodes in 3.8% of MA patients versus 5.8% of controls; 3) PAD in 30.7% of both MA patients and controls; 4) agoraphobia with or without PAD in 50.0% of MA patients versus 48.1% of controls; 5) social phobia in 7.7% of both MA patients and controls; and, 6) generalized anxiety disorder in 30.8% of MA patients versus 38.5% of controls.
Conclusion We did not find any statistically significant differences. Our findings appear at a variance with those reported so far by other authors, who suggested a close correlation between MA and mood and anxiety disorders, in particular PAD.

P 3086

The Spectrum of Headaches experienced by Migraineurs in a primary care setting

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Introduction This prospective, international, open-label study was designed to examine the association of headache impact and migraine diagnosis in subjects presenting with headache to primary care physicians (PCP). The spectrum, impact and the frequency of IHS migraine, migrainous, and tension headaches was also determined.
Method Newly diagnosed migraine (n=271) and non-migraine subjects (n=105) completed a headache impact test and headache survey at baseline, and diaries for the first 6 headaches treated during the study. At study completion an expert panel reviewed the diaries, providing a final IHS diagnosis. The number of attacks subjects experienced meeting criteria for migraine (1.1/1.2), migrainous (1.7), or tension headache (2.1) was also determined.
Results Diary review by the panel resulted in the following diagnostic groups: non-migraine (n=22), misdiagnosed migraine (n=86), and migraine (n=265). The spectrum of headache and percentage of attacks experienced were: in the mi-

graine diagnosed group: 51% migraine (1.1), 22% migraine (1.2), 23% Migrainous (1.7) and 4% Tension headache (2.1). In the misdiagnosed group results were: 26% migraine (1.1), 10% migraine, (1.2), 47% migrainous and 17% tension headache. Misdiagnosed cases were 2–3 times as likely to have migrainous or tension headache. Using diary data, the misdiagnosed and migraine groups were similar in reporting moderate or severe headache pain, both at 91%. Misdiagnosed cases were more likely to report bilateral pain.
Conclusion Migraineurs experience a spectrum of headaches. Diagnostic errors are more likely to occur when one focuses on headache frequency instead of the migraine features of headache.

P 3087

Association of headache impact test (HIT-6) and IHS migraine diagnosis in the primary care setting

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Introduction This prospective international study examines the association of headache impact and IHS migraine diagnosis in subjects presenting with headache to primary care physicians (PCP).
Method Subjects not previously diagnosed with migraine (N=377) completed baseline and monthly HIT-6 and diaries for three months. At study end, experts blinded to HIT-6 score reviewed the diaries and provided a final IHS diagnosis. The accuracy of HIT-6 in identifying IHS 1.1 or 1.2 migraine diagnosis were evaluated by receiver operating characteristics (ROC) curve, sensitivity, specificity, positive and negative predictive values for HIT-6 scores of 56, 60 and 63.
Results 76% of subjects received IHS migraine diagnosis after expert review. The full range of HIT-6 scores (36 to 78) has a diagnostic accuracy (area under the ROC curve) of 67%. The probabilities of migraine diagnosis for HIT-6 scores >/=56, >/=60 and >/=63 were 0.80, 0.82 and 0.84, respectively (positive predictive values). The percentages of migraineurs having a score >/=56, >/=60 and >/=63 were 91%, 85% and 67%, respectively (sensitivity). The probabilities of non-migraine were 0.46, 0.44, and 0.36 for scores <56, <60 and <63, respectively (negative predictive values). The percentages of non-migraine subjects having a score <56, <60 and <63 were 25%, 39% and 60%, respectively (specificity). Using a cut-off score of 60, HIT-6 identified migraine diagnosis correctly 74% of the time.
Conclusion Subjects with high HIT-6 scores are likely IHS migraineurs. Patients with migraine features who report low HIT scores may require additional clinical evaluation. HIT-6 may facilitate migraine diagnosis in the PCS.

P 3088

Increased time at work and improved productivity while at work with Rizatriptan 10 mg: a multi-work site study in Spain (MILEBA)

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Introduction The objective of our study was to examine the impact of rizatriptan 10 mg on work and productivity in employed migraine sufferers.
Method Employed individuals with migraine (IHS criteria), at 20 companies with 27 work sites, were recruited by the on-site Occupational Medicine Specialists in a prospective study. Patients were administered a questionnaire with a 3 month recall period at baseline and at a 3 month follow-up visit on their experiences with rizatriptan pre/post intervention. Work-related outcome measures included work missed due to absence, percent effectiveness in paid work performance, productive time on the job, and total work loss due to migraine. Wilcoxon tests were used to compare work-related outcomes.
Results A total of 259 patients (68.5% female, mean age 39 years, 75.1% without aura) completed the study. Pre-intervention treatments used by patients prior to exposure to rizatriptan 10 mg were: 78.8% paracetamol or composed analgesics, 45.2% NSAIDS, 33.2% ergotamine, and 17.8% others. Mean changes in work-related outcome measure for 3 month recall period pre and post intervention were: days absent from work (1.86 vs 0.6, p<0.001); percent effectiveness in paid work performance (57.3% vs 69.2%, p<0.001); productive time lost while on the job (3.4 vs 1.5 days, p<0.001); and total work day equivalents lost due to migraine (5.2 vs 2.1, p<0.001).
Conclusion In an employed population of migraine sufferers, treatment with rizatriptan 10 mg significantly decreased (>60% reduction) total migraine-related work loss compared to their experiences with previous medications. These findings have important implications for selecting appropriate treatment in a disabled employed migraine population.

P 3089

Improved quality of life with Rizatriptan 10 mg vs previous migraine treatment in an employed population: a multi-work site study in Spain (MILEBA)

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Introduction The objective of our study was to assess the impact of rizatriptan 10 mg on quality of life in employed migraine sufferers primarily using other acute treatments.
Method Employed individuals with migraine (IHS criteria), at 20 companies with 27 work sites, were recruited by the on-site Occupational Medicine Specialist in a prospective study. Patients were administered a generic quality of life questionnaire (SF-36) at baseline to record their quality of life while on previous migraine treatment and at a 3 month follow-up visit to record their quality of life after treatment with rizatriptan 10 mg. Wilcoxin tests were used to compare post-intervention to pre-intervention quality of life scores.
Results A total of 259 patients (68.5% female, mean age 39 years old, 75.1% without aura) completed the study. Pre-intervention treatments used by patients prior to exposure to rizatriptan 10 mg: 78.8% paracetamol or composed analgesics, 45.2% NSAIDS, 33.2% ergotamine, and 17.8% others (6.5% of all patients had previously used a triptan). Comparing post-intervention to the pre-intervention SF-36 scores, we observed significant improvements (p<0.001) in the overall 5 out of 8 domains (physical functioning, bodily pain, vitality, social functioning, and mental health).
Conclusion Treatment of migraine with rizatriptan 10 mg significantly improved quality of life compared to patient experiences with previous migraine treatment in a cohort of employed migraine sufferers.

P 3090

Changes in head motion after saline induced neck pain

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Introduction In previous studies the kinematic analysis of painful head movements in patients showed characteristic changes in velocity, amplitude, synkineses, acceleration and deceleration. The aim of the present study was to investigate the amount and duration of these changes in healthy volunteers after pain stimulation by injection of hypertonic saline.
Method 12 volunteers participated in the study (six females; six males; age range: 22–30 years; mean: 26 years). The head movements were recorded by Cervicomotography (Berger 1990), a method using a magnetic field measuring system (Flock of Birds) and special software programmes. 0.5 ml hypertonic sa-line was injected paravertebrally right of the seventh cervical vertebra. A one minute lasting head rotation was measured three times before the injection, immediately after the injection and one, three and twenty-four hours after the injection. The course of pain intensity was recorded by a visual analogue scale.
Results The saline induced pain lasted from 3 to 7 minutes with a medium duration of 4.5 minutes. 1 and especially 3 hours after the injection a significant reduction of the range of movement (ROM) was seen. Significant changes could be detected in other kinematic parameters too, as mean maximum velocity, mean velocity, pain inhibition, harmony of movement etc. Only after 24 hours all parameters have returned to their baseline.
Conclusion It could be clearly demonstrated that movements remain changed even after the pain has already subsided.

P 3091

Lamotrigine for chronic neuropathic pain

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Introduction Lamotrigine is an anticonvulsant with pharmacological actions that include activity in blocking voltage-gated sodium channels, as well as several blocking activities at calcium channels (N and P-type). These mechanisms of activity have been shown to be useful in pain and headache in many compounds that possess them. I chose to evaluate lamotrigine in a population of refractory chronic pain patients.
Method 35 patients (25 males, 10 females) were given lamotrigine as an add-on medication for their painful symptoms. All had some form of neuropathic pain: 21 had cervical or lumbosacral symptoms; 3 had facial pain; 5 had complex regional pain syndrome pain; 4 had diabetic or other endocrinopathic pain; 2 had neuroma pain. All had failed at least two or more other attempts at treatments with neuronal stabilizing agents for their pain.
Results Patients rated their pain on a 0 to 10 numeric rating scale (NRS). Average length of treatment was 4 months or more. Average dose was 260 mg per day. The average reduction in pain scores, rated on a NRS, was 70.9% in 14 patients. 6 patients were non-responders, and 2 were dropped due to side effects (drowsiness and rash). 5 were lost to follow up or did not follow the titration schedule accurately and 8 were just started on lamotrigine.
Conclusion Lamotrigine was found to be an effective agent for refractory neuropathic pain syndromes with an excellent margin of safety and tolerability in this open-label study. Further double-blind studies are warranted with this agent.

P 3092

Intradermal Botulinum toxin, type B, treatment for cervicogenic migraine

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Introduction Botulinum toxin, type B, is primarily used intramuscularly for a number of disorders, including spasm and headache. This study used intradermal sites of administration of the toxin to study its effect in cervicogenic migraines. This is based on the high concentration of nociceptive fibers in the skin and the possibility that cutaneous inputs from the cervical region may contribute to these migraines.
Method 10 patients were given open-label botulinum toxin, type B, intradermally. All had unilateral IHS-criteria migraines with muscle spasm; 4 had failed cervical surgery and all had known cervical structural pathology by MRI. 2500 or 5000 units of type B toxin were given intradermally by raising a skin wheal on the side of the migraine at the level of the greater and lesser occipital nerve inlets.
Results 5 patients reported a significant decrease in migraine frequency, at least 75%. Spasm was also reduced to the same or greater amount. 3 of these patients reported greater than 90% reductions and average duration of effect was 16 weeks (range= 10–24 weeks). 2 patients did not have any significant change in migraine pattern, and 3 were just injected. Remaining migraines were easier to abort. One patient reported transient flu-like symptoms.
Conclusion This study shows the effectiveness of a new site of delivery of botulinum toxin, type B, in treating cervicogenic migraines. Intradermal delivery suggests, speculatively, anterograde transport of toxin to the dorsal horn in nociceptive fibers where pain transmission may be blocked via any number of mechanisms, including central sensitisation, windup and blockade of specific facilitatory neuromodulators. Double-blind studies to replicate these open-label findings are warranted in the study of botulinum toxin, type B.

P 3093

Pain responsiveness in cervical dystonia: different doses of Botulinum toxin type-a

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Introduction Effectiveness of Botulinum Toxin Type-A (BTX-A) against pain associated with cervical dystonia has been established. However, several studies suggest that a direct antinociceptive effect distinct from reduction in muscle spasm may be involved in this process. The aim of the present study was to investigate the effectiveness of different doses of BTX-A in pain associated with cervical dystonia.
Method We studied 31 patients with painful cervical dystonia (age range 24–63 years). Using a randomised, double-blind, cross-over design (3 treatment periods of 4-month duration) we injected patients with three different doses of BTX-A (50, 100 and 150 U of BTX-A as BOTOX) in the most affected muscles. The patients' baseline level of pain and the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) were assessed.

Clinical assessments were performed each week during the 12-month study. Side effects were monitored during the study.
Results Our results showed that significant pain relief (p 0.05) was obtained in patients during each treatment period (50, 100, and 150 U) already one week after injection. On the contrary, TWSTRS-Total score was significantly decreased at 2-weeks post injection, but only during two treatment periods with higher doses of BOTOX (100 and 150 U). The major benefit of BTX-A application on pain reduction compared with dystonia improvement was the duration of action and the lower beneficial dose. No systemic side effects were noted during the study.
Conclusion Our results appear to demonstrate for the first time that BTX-A may have a direct antinociceptive effect distinct from the effect on muscle relaxation.

P 3094

Primary headache disorders – analysis of 2816 patients in a Turkish population

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Introduction Primary headache disorders (PHD) show cultural and geographical variations in both frequencies of subtypes and clinical characteristics. The aim of this study was to provide the frequency, sex ratio, age distribution and clinical characteristics of subtypes of PHD diagnosed according to the criteria of International Headache Society (IHS) in a Turkish population.
Method A retrospective study was conducted in the neurology outpatient clinics of the hospital of Süleyman Demirel University Medical Faculty, Isparta, Turkey, between the years of 1994 and 1999. A total of 2816 patients admitted to the hospital with headache and were diagnosed PHD on the basis of IHS classification.
Results Of the 2816 patients 2342 (83%) being female and 474 (17%) male; 926 (32%) were diagnosed chronic tension-type headache, 925 (32%) migraine without aura, 696 (25%) episodic tension-type headache, 126 (4%) migraine with aura and 143 (7%) other disorders. Mean age of all patients was 38+/–13.7 years. There was preponderance in females of all the subgroups of disorders. The most frequent group of prodromal symptoms were psychosomatic symptoms and mood changes in patients diagnosed migraine without aura, chronic tension-type head-ache and episodic tension-type headache. Precipitating and improving factors showed great similarities in all of the four groups of disorders.
Conclusion Our study demonstrates a higher frequency of chronic and episodic tension-type headaches than expected. Female predominance in all subgroups of PHD and the clinical characteristics of disorders are consistent with Western literature.

P 3095

Changes in headache frequency in Greek recruits during basic training period

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Introduction The aim of our study was to present part of an observational study concerning epidemiology of headaches among Greek National Service recruits. In the present part, we investigate for changes in migraine and tension-type headache recurrence frequency during basic training period, among those who reported headaches with the corresponding features on a regular basis.
Method We asked 2130 recruits (age range 18–33) the single question of "having being experiencing at least 1 headache every 3 months in their previous life". Those who gave an affirmative answer were interviewed through a 30-points questionnaire investigating type and frequency of their headaches. Questions concerned the 3-months period during the same season of time 1 year ago, and the 3-months period of their basic training. According to our questionnaire, we classified subject's headaches in 3 groups; migraine, tension headache and other or not identifiable type. In this presentation, we have excluded the latter group, as well as data concerning newly-presented headaches, and changes in type of headache during the follow-up. Comparisons involved headache recurrence frequency between the two periods, among subjects with migraine and tension headache. We adjusted our data for possible confounding by change of climate (highland to lowland).
Results In our study, 298 subjects reported headaches. The characteristics that emerged from their answers allowed us to positively identify 77 subjects with migraine (age range 18–31), and 154 with tension headache (age range 19–30). Headache recurrence frequency was significantly increased among tension-type group (70 subjects showed no change, 52 showed increase and 32 showed decrease in headache recurrence frequency, P=0.029). Subjects with migraine did not show any significant change (only a trend for increase) in the recurrence frequency of their condition (47, 17, and 14, respectively, P=0.059).
Conclusion It seems that a physically and psychologically stressful condition, such as basic military training of National Service recruits, does not act significantly on the frequency of migrainous headaches. On the other hand, the frequency of tension-type headaches tends to aggravate. Considering psychological factors, these results add to the body of evidence for the organic origin of migraine, in comparison with tension-type headaches.

P 3096

Prevalence of migraine and tension-type headache among primary and secondary school students in Belgrade-Yugoslavia

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Introduction Most migraine and tension-type headache studies in children and adolescents are clinic-based, and therefore tend to underestimate its real prevalence. On the other hand, in the most population-based studies diagnosis was made by questionnaire based on International Headache Society criteria, so restrictive in paediatric migraine. The objective of our study was to estimate the lifetime prevalence of migraine and tension-type headache in primary and secondary school students in Belgrade.
Method A total of 1663 primary school students (age 7–15 years) and 3605 secondary school students (age 15–19 years) answered the question about recurrent headaches during life. Diagnosis of idiopathic or symptomatic headaches, in the sample of patients with reported recurrent headaches was made by clinical interview and examination done by neurologist (headache specialist).
Results Of 413 students with recurrent headaches, idiopathic headaches occurred in 76.7% of primary school students, and in 80.2% of secondary school students. The lifetime prevalence of

migraine in those aged 7–15 years was 3.5%, and in 15–19 aged 3.7%. The lifetime prevalence of tension-type headaches was 2.0% and 2.8%, respectively. Female to male ratio of migraine prevalence in primary school students was 1.7 and in secondary school students 2.7 ($p<0.01$). Female to male ratio of tension-type headache prevalence did not change significantly with age (1.5 and 1.3; $p>0.05$).

Conclusion Our results proved that migraine and tension-type headache are very frequent among the population aged 7–19 years. The migraine prevalence from childhood to adolescence did not change significantly, but the female to male ratio became higher in adolescence.

P 3097

Familial hemiplegic migraine – case report

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Introduction Familial hemiplegic migraine (FHM) is a rare disorder in which the migrainous attacks are marked by the occurrence of transient hemiplegia, often with other neurological deficits including sensory symptoms, appearing before or during the headache. The episodes are similar in all affected members of the family. It has an unknown pathogenesis, and the gene responsible for this autosomal dominant disease was mapped to chromosome 19p13.

Case report A 21-year-old male, previously diagnosed as having partial epilepsy and on carbamazepine, was admitted due to episodes since 7 years old comprising vision disturbance with sparkling scotoma and left hemiparesis for 20–30 minutes. An intense, sometimes throbbing, frontotemporal bilateral headache, with nausea/vomiting and phono/photophobia, followed this clinical picture. The headache usually was lasting 4–5 hours and was often refractory to non-steroid anti-inflammatory drugs. Interictal neurological examination was normal. Cerebral magnetic resonance was normal and EEG showed nonspecific changes on right occipital region. The patient has a familial history of 6 similar cases with an autosomal dominant pattern. It was possible to observe his father (50 y.o.) and brother (15 y.o.), both with a previous diagnosis of partial epilepsy and on carbamazepine, and confirmed the stereotype of the episodes.

Conclusion FHM may be mistaken by other neurological entities that course with transient focal neurological dysfunction and headache, as occurs with partial epilepsy and transient ischemic attacks. The correct characterization of each episode is very important, allowing a correct diagnosis and therapeutic management. In this particular case the accurate anamnesis suggests FHM.

P 3098

Importance of the inflammation mechanisms in the vascular headaches

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Introduction Migraine pain caused by regional decrease of cerebral blood flow develops mild ischemia and inflammation with releasing of free radicals acting on pain inducing receptors. This study aimed at investigating the role of inflammation in developing migraine.

Method 114 patients, aged 10 to 25 years were investigated. Control comprised of 40 healthy individuals, transcranial Dopplerography was conducted 4 times. The mixed culture of autologous lymphocytes (MCAL) was investigated according to the method of Hafler et al. 1974. Count of blast transformed lymphocytes defined in controlling and experimental cultures was processed by "mythomicin-C". Levels of IL-1β and TNF-α were studied by enzyme-linked immunosorbant assay (ELISA). T-paired test was used for statistical evaluation.

Results In attack-free periods 88% of patients did not reveal changes in MCAL compared to control. Count of blast transformed lymphocytes in 72% of patients was significantly reduced (1.5 ± 0.1 versus 8.0 ± 1.1 $P<0.01$). The level of IL-1β was significantly higher in 32.7% of patients (24.2% with unilateral and 6.8% with bilateral carotid siphon spasm) compared to control (157 ± 113pg/ml versus 482 ± 154 pg/ml p,0.01), while the TNF-α did not show significant changes. During attack periods the level of IL-1β was elevated (482 ± 154pg/ml versus 335 ± 178 pg/ml $P<0.5$) in 35.4% (29% with unilateral and 4.1% with bilateral carotid siphon spasm). TNF increased without statistical significance in 44% of patients.

Conclusion Patients with unilateral and bilateral carotid siphon spasm were found to have elevated levels of IL-1β and autoimmune reactions this can result in production of immune complexes and toxic free radicals impacting the pain-inducing receptors.

P 3099

Migraine and co-morbidities

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Introduction It is not uncommon with migraineurs to find symptoms of other disorders which "accompany" migraine. These "co-morbidities" are often precipitants of a migraine attack.

Method In studies carried out in the Dept. of Neurology, Clinical Health Centre in Rijeka, we analysed randomly the case history of 250 migraineurs. We established the presence of "co-morbidities of migraine" in 80 migraineurs (32%) irrespective of gender and age. Diagnosis of migraine was made on the basis of IHS classification.

Results In a group of subjects with "co-morbidities" the following was expressed in percentages:

– pains in neck musculature, interscapular pain and fibromyalgia were present in 27 (33.75%) migraineurs.
– insomnia: most commonly with apnoea during sleep in 15 (18.75%).
– gastric disorders: gastritis, duodenal ulcer in 12 (15%).
– arterial hypertension in 11 (13.75%).
– bronchial asthma, chronic bronchitis and allergic diathesis in 10 (12.5%).
– depressive syndrome in 7 (8.75%).
– epilepsy in 5 (6.25%).
– diabetes in 5 (6.25%).
– migrainous stroke in 3 (3.75%).

We noticed a relatively high presence of myalgic discomfort with a somewhat lower level of insomnia combined with other psychological and psychiatric disorders, which point to the longstanding stated hypothesis on the existence of a "migrainous personality". Next is migraine accompanied by arterial hypertension and then disorder of the respiratory tract (allergic diathesis). Migraine accompanied by epilepsy has been shown to be rare in our studies.

Conclusion The results of our studies are compatible with recent literature.

P 3100

Head image disorder in patients with various chronic headache syndromes

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Introduction Headache and migraine constitute a multidimensional experience with painful, emotional and cognitive aspects. The head image projected on the body schema is a person's subjective representation against which the integrity of the neck/head is judged. It appears that many patients with chronic and episodic headache have a distorted size, shape and awareness of the head.
Method A questionnaire was designed, including the epidemiology, character and severity of headache, the Beck depression scale and a sub-scale with 10 descriptors typifying different distortions of head image.
Results 53 consecutive patients were included in our pilot study: 31 migraine patients, 9 patients with tension headache, 6 patients with mixed headache and 4 patients with trigeminoautonomic cephalalgia. 87% of migraine patients and 66% of tension type headache patients reported various distinct head image disorders. Whereas the patients with tension type headache reported increased size and weight solely during the headache episode, patients with migraine had unusual distortions such as unawareness of parts of the head, changes in position of the ear/temples, and reduplicative phenomena. The migraine patients rated their distress with regard to this experience as significant. Additionally, their experience either preceded or followed the headache phase. No significant correlation between the Beck depression scale and the presence of the head image disorder was found. However, the degree of distress correlated with depression.
Conclusion Head image disorder is common among patients with headache and more so among migraine patients. This experience outlasts the headache phase and generates considerable distress.

P 3101

Review of gabapentin dosing in five placebo-controlled clinical trials for neuropathic pain

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Introduction Gabapentin was studied for the treatment of neuropathic pain in five double-blind, placebo-controlled, multicenter studies. The objective of our study was to investigate the relationship between gabapentin dose and neuropathic pain reduction.
Methods 1357 patients with painful diabetic neuropathy (two studies), post-herpetic neuralgia (two studies), and neuropathic pain of various etiologies (one study) were analysed. The studies utilized a 3–4 week dose titration period followed by 4 weeks at fixed dose (600–3600 mg/day). Patients rated their pain daily using an 11-point Likert scale.
Results Gabapentin, at doses between 1800 and 3600 mg/day, led to lower mean daily pain scores compared with placebo levels. Additionally, more patients had a 50% or greater improvement in pain scores on gabapentin. Both measures tended to improve with increased dose up to the maximum of 3600 mg/day. Efficacy was sustained for the duration of the studies. Older patients had a somewhat greater treatment effect, possibly due to increased drug exposure related to decreases in renal clearance or changes in GI transit times. Race and gender did not influence the treatment effect.
Conclusion Gabapentin, at a dose range of 1800 to 3600 mg/day, produces a sustained and dose-dependent reduction in neuropathic pain. The effect is enhanced in older patients and appears to be correlated with gabapentin exposure.

P 3102

Epidural corticosteroid injections in management of the sciatica

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Introduction Epidural injections are the main focus of interest in management of sciatica, after the period of back surgery development.
Methods In patients with sciatica after 4 weeks of unsuccessful conservative management or in patients with failed back surgery syndrome epidural injections of local anaesthetics and depot preparations of corticosteroids were recommended. There were 1214 patients managed by lumbar epidural injections. We apply corticosteroid, local anaesthetics and normal saline in the epidural space. We performed caudal route epidural injections in 268 patients during 4 years.
Results In comparison of a group of patients with epidural injections to the control group we found significant improvement in the former group of patients. The effect of caudal route of epidural injections was evident mainly in patients who had undergone back surgery.

P 3103

How to treat the patients with low back pain?

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Introduction The aim of the study was to determinate the efficacy of therapeutic approaches in patients with low back pain (LBP). The results of LBP treatment are far from the ideal.
Method Consecutive patients with non-acute (one month duration) LBP were divided into 2 groups: with and without sciatica. The treatment included 3 stages: A. Anti-inflammatory drugs (NSAIDs) at the beginning; B. Single spinal manipulation; C. Therapeutic complex included repeated spinal manipulations, massages, electrical stimulation, electromagnetic fields, and low-power cold infrared laser (twice a week, for 4 weeks). Self-report method was used for treatment evaluation. The results were compared after each stage of the treatment. Chi-square test was used for statistical analysis.
Results 79 patients had LBP without sciatica (Group 1), and 46 patients suffered from the LBP with sciatica (Group 2). Alleviation of the LBP after NSAIDs using was reached in 63 (79.7%) patients without sciatica, and in 17 (37.0%) patients with sciatica, OR=6.7 (CI=4.1–8.3), $p<0.001$. LBP improved after single spinal manipulation in 32 (40.5%) patients in Group 1 and in 19 (41.3%) patients in Group 2, differences were statistically non-significant (ns). Complex treatment was successful in 64 (81.0%) patients without sciatica and in 37 (80.4%) patients with sciatica, (ns).
Conclusion NSAIDs were effective in the patients without sciatica, but had low efficacy in the patients with sciatica. Single spinal manipulation was not so effective in the patients with or

without sciatica. Complex therapy was very potent approach in all patients with non-acute LBP.

P 3104

Levetiracetam as treatment for chronic pain

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Introduction Levetiracetam, a new anticonvulsant with effects that block high voltage (N-type) calcium channels, has recently been shown by the author to be useful for the treatment of migraines.
Method 38 patients were selected from a chronic pain population. Most (n=35) had failed 2 or more prior attempts using other agents to treat painful symptoms. 28 were on such therapy at the time levetiracetam was added. 22 had radicular neck or back symptoms due to disc disease or failed surgery; 6 had diabetic neuropathy and 5 had complex regional pain syndrome, type 1. 4 had carpal tunnel syndrome or other peripheral nerve entrapment; 1 had facial pain. All patients rated the severity of their pain on a 0 to 10 numeric rating scale (NRS). Levetiracetam was begun at 250 mg in the evening; doses were increased every 3–5 days. Dosing range was 1500–6500 mg, with an average duration of treatment of 8.5 months.
Results 10 patients reported an average 69.4% reduction in their NRS pain scores with levetiracetam. Another 6 reported 25–50% reductions in pain while 4 reported less than 25% reduction. 5 patients dropped out due to side effects (3=nausea, 2=drowsiness), 4 were noncompliant or lost to follow-up and 9 are in the early titration phase.
Conclusion This study shows efficacy of treatment of chronic neuropathic pain with levetiracetam. This agent is well tolerated and may offer an alternative to other neuronal stabilizing agents, either as a primary medication or as add-on therapy. Further studies, using double-blind methods, are warranted.

P 3105

Zonisamde as a treatment for chronic pain syndromes

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Introduction Zonisamide has pharmacological activity in blocking sodium channels, T-type calcium channels and in modifying serotonergic and dopaminergic transmission. It may be useful in treating chronic pain.
Method 42 patients with chronic neuropathic pain disorders were treated with zonisamide in an outpatient setting. 28 had cervical/lumbar discogenic pain, including failed surgeries; 5 had complex regional pain syndrome; 6 had nerve entrapment syndrome pain; 3 had facial pain syndromes. Zonisamide was begun at 100 mg every fourth night (for 4 doses), with progression to every third night (for 5 doses) and then every other night. Further dosing changes were made every 2–3 weeks. 38 patients had failed 2 or more prior attempts and 37 were on such therapy when zonismide was started. Each patient rated his or her pain severity on a 0 to 10 numeric rating scale (NRS), together with duration of pain in hours.
Results 26 of 42 patients treated with zonisamide reported improvement in pain scores: 10 patients (24%) reported a better than 60% reduction in daily pain scores; 8 patients reported 30–60% reductions and 8 reported less than 30% reductions. Only 2 patients were lost due to side effects (drowsiness); 4 were lost to follow-up, 8 did not respond to therapy and the balance have just been started. 15 patients were able to taper or stop their existing anticonvulsant therapy.
Conclusion Zonisamide may provide an alternative for treatment of refractory neuropathic pain in a difficult-to-treat patient population that has failed prior attempts. Double-blind studies are warranted with zonisamide.

P 3106

Spinal nerve root stimulation in radicular pain

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Introduction During the last three decades spinal cord stimulation (SCS) has progressed continuously but in some cases SCS is not sufficient for pain control, e.g. due to postoperative epidural fibrosis. An alternative to SCS could be the method of nerve root stimulation (NRS).
Method Lead placement for NRS is performed similar to the SCS-technique, but the epidurally introduced lead is forwarded in caudad direction toward the neural foramen of the affected nerve root. The electrode is forwarded through the neural foramen and is placed partly in the extraforaminal space. Lead implantation is carried out percutaneously, after test stimulation a battery powered, telemetrically programmable stimulator is implanted.
Results In 12 patients with monoradicular, lumbar/sacral pain due to postoperative epidural fibrosis we attempted to carry out NRS. 3 times the lead could not be introduced into the caudad-epidural space, 3 times the electrode could not be guided into the neural foramen due to major fibrosis. In 6 cases the electrode could be placed in the neuro-foramen and forwarded to the lumbo-sacral nerve plexus. Test stimulation provided optimal stimulus sensation with high-grade (80%) pain reduction and patients consecutively were provided with an internalised stimulation system.
Conclusion Benefit of NRS compared to SCS is a higher degree of pain alleviation, constant stimulus sensations, less lead displacements and lower energy consumption.

P 3107

Occipital neuralgia relieved with C2 ganglion radiofrequency lesioning – case report.

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Introduction Occipital neuralgia is the term used to describe chronic occipital pain which can be a condition associated with migraine, tension headache, cervical strain and cervicobrachial syndrome, however idiopathic occipital neuralgia is characterized by paroxysmal, electric shock-like pain from the occipital region to the vertex of the head. The exact mechanism, which causes such pain syndrome, is not known.
Case report The 42 years female patient was referred to our hospital with a seven-year history of severe right occipital neuralgia. The medication therapy such as non-steroid analgesics, carbamazepine, gabapentin, and diazepam was without benefit. She was also treated with local anaesthetics and steroids infiltration with some short-term improvement, which lasted a maximum of a few days. X ray examination of the cervical spine and scull, EMG and MRI of the head and cervical spine revealed no lesion or any sign of compression of relevant anatomical structures. Routine biological investigations, including those for blood and urine levels of calcium phosphate, magnesium and serum creatine kinase, were normal. She underwent right C2 ganglionectomy and in the seven-month follow up period she has no recurrence of pain.

Conclusion Patients with idiopathic occipital neuralgia who have not experienced improvement after medical treatment became the candidates for surgical therapy. Ganglionectomy C2 in idiopathic occipital neuralgia is a very effective and low risk surgery.

P 3108

Spinal nerve root stimulation in radicular pain due to postoperative epidural fibrosis

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Introduction Epidural spinal electrical stimulation (ESES) has been improved continuously during the last 30 years, although still the result of stimulation in some cases is not satisfactory. In case of monoradicular pain, e.g. due to postoperative epidural fibrosis, the patient would need stimulus sensations for pain control in the respective dermatome, which cannot be guaranteed in all cases of ESES treatment. An alternative to ESES is the direct stimulation of the affected nerve root.
Method Lead placement for nerve root stimulation (NRS) is performed similar to the ESES-technique, but the epidurally introduced lead is not forwarded in cranial but in caudad direction toward the neural foramen of the respective (affected) nerve root. The lead tip (electrode) can be forwarded through the neural foramen and the electrode can be placed partly in the extraforaminal space and stimulation in this case also can provide a plexus stimulation. With this technique only lower lumbar (L3–L5) and sacral (S1–S4) nerve roots can be treated. Lead implantation is carried out percutaneously, after a test stimulation period of 3 days to one week a battery powered stimulator is implanted. Stimulation parameters can be programmed telemetrically.
Results NRS was attempted to be carried out at our institution in 12 patients with monoradicular, lumbar and sacral pain due to postoperative epidural fibrosis. In 3 cases the lead could not be introduced into the epidural space in the described caudat directed way, in 3 other cases the electrode could not be guided properly into the neural foramen due to major fibrosis. In these 6 cases the procedure was changed to ESES. In the rest of the cases the electrode could be placed into the neural foramen and in four cases also forwarded through the foramen to the lumbosacral nerve plexus. Test-stimulation provided optimal stimulus sensation with high-grade (80%) pain reduction. In all this cases consecutively a stimulation system was internalised too. These patients undergo NRS for a period of 2 months to 2 and a half years with 8 month in mean.
Conclusion The benefit of NRS compared to ESES is the higher degree of pain alleviation, the achievable constant stimulus sensations, less electrode displacements and lower energy consumption.

Ageing and dementia 2

P 3109

Use of the MOSES and NPI/NH to assess the effects of olanzapine treatment in patients with Alzheimer's disease-associated psychosis

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This pilot study was conducted to compare changes in dementia measured with the Multidimensional Observation Scale for Elderly Subjects (MOSES) and the Neuropsychiatric Inventory-Nursing Home version (NPI/NH) scales.
Elderly patients (n=41 for all measures) with psychosis associated with Alzheimer's disease (AD) received olanzapine (1.0–7.5 mg/d) for 10 weeks. The MOSES scale was used to assess functional impairment, the NPI/NH total score was used to assess psychopathology, and the sum of the NPI/NH *Delusions* and *Hallucinations* subscores (Psychosis Total) was used to assess changes in psychosis.
Following treatment with olanzapine, mean LOCF change scores showed significant improvement on the Psychosis Total (–9.73±6.43; p<.001), MOSES (–14.59±14.96, p<.001), and NPI/NH total (–36.54±21.67, p<.001). Pearson correlation analyses showed a significant correlation between baseline MOSES and NPI/NH total scores (r=0.5472, p<.001). Correlation between endpoint MOSES and NPI/NH total scores approached, but did not achieve, significance (r=0.2925, p=.06). No other significant baseline-, endpoint-, or change-score correlations were seen among the MOSES, NPI/NH total, or Psychosis Total scores.
These data indicate that olanzapine effectively reduced levels of psychosis and overall impairment in elderly patients with AD. The MOSES and NPI/NH scales may be useful indices of impairment, but external consistency between them is low.

P 3110

Donepezil in advanced Alzheimer's disease: Improvements in cognition and quality of life. Results of the 2nd German post marketing surveillance study

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Introduction Donepezil is approved for the symptomatic treatment of mild to moderate Alzheimer's disease (AD) in over 50 countries. Here we report results from the second German post marketing surveillance study, in which patients were observed while switched from other antidementia treatments (i.e. nootropics) to Donepezil. The tolerability and efficacy of Donepezil in advanced AD patients (mini-mental state examination [MMSE] score ≤10) were evaluated in comparison with patients in milder stages of the disease.
Methods 913 patients were enrolled. Cognition was evaluated by the MMSE. Quality of life (QoL) was assessed by the investigators on a three-point scale (improved/unchanged/worsened). Tolerability was evaluated by adverse event (AE) reports.
Results A baseline MMSE was documented for 906 patients; 76 had a baseline MMSE of ≤10 ("severe" cohort, mean baseline MMSE 7.3). The "moderate" cohort (MMSE 11–18) comprised 377 patients (mean MMSE 15.0) the "mild" cohort (MMSE ≥19), 453 patients (mean MMSE 22.3). After 3 months of Donepezil therapy, MMSE score improved by +3.0 points in the "severe" cohort ("moderate": +2.8, "mild": +1.5). QoL was judged "improved" in 65.3% of the "severe" cohort ("moderate": 68.9%, "mild": 71.2%). Donepezil was very well tolerated. AEs were reported in 6 patients (7.9%) of the "severe" cohort ("moderate": 6.6%; "mild": 10.4%).
Conclusions In a routine clinical setting reflecting daily life conditions, Donepezil showed at least the same improvements in cognition and QoL in advanced to severe Alzheimer patients as in patients with mild to moderate AD. Donepezil was very well tolerated across all severity cohorts.

P 3111

Further understanding the meaning of "clinical benefit": Results from the pre-randomisation phase of the Donepezil AWARE Study

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Background Alzheimer's disease (AD) patients who show no apparent improvement after 3–6 months are often discontinued from cholinesterase inhibitor therapy. However, due to the degenerative nature of AD, these patients may still experience therapeutic benefits.
Objective To determine the extent to which donepezil-treated AD patients show clinical benefit, based on criteria requiring evidence of improvement.
Design AWARE (Aricept WAshout and REchallenge) consists of 3 phases: 1) 24-week, pre-randomisation, open-label phase; 2) 12-week, randomised, double-blind, placebo-controlled phase; 3) 12-week, single blind Donepezil treatment phase.
Methods (pre-randomisation phase) All patients received Donepezil 5 mg/day for 28 days, then 10 mg/day. Clinical benefit was assessed at Weeks 12, 18, and 24. Patients classified as showing "no clinical benefit" exhibited decline or no change from baseline on the MMSE and the physician was not sufficiently certain of clinical benefit to warrant continued treatment (assessed by formal questionnaire); these patients were randomised into the double-blind phase.
Results 817 patients (mean MMSE, 20.7) were enrolled. After 24 weeks, 51% of patients were rated as showing "clinical benefit", (MMSE mean change from baseline, 2.3); 25% were rated as showing "no clinical benefit", (MMSE mean change from baseline, –1.8). 24% discontinued; 15% due to adverse events.
Conclusions The proportion of patients showing "clinical benefit" within 24 weeks was high. Patients who declined or showed no change continued in the double-blind phase of AWARE. Although these patients were rated stringently in this 24-week phase as showing "no clinical benefit", they may still prove to benefit from long-term treatment with Donepezil.

P 3112

Donepezil improves cognition in patients with vascular dementia

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Background Evidence to suggest that patients with vascular dementia (VaD) may benefit from treatment with cholinesterase inhibitors is accumulated.
Objective Evaluation of the efficacy and tolerability of the acetyl cholinesterase inhibitor Donepezil in patients with probable or possible VaD.
Design A randomised, double-blind, placebo-controlled, 24-week, parallel group study (Study 307).
Methods A diagnosis of probable or possible VaD according to NINDS-AIREN criteria was required for inclusion. Patients with a prior diagnosis of Alzheimer's disease were excluded. Patients were randomised to receive placebo, Donepezil 5 mg/day or Donepezil 10 mg/day (5 mg/day for first 28 days). Efficacy assessments included the ADAS-cog. Results are reported for intent-to-treat observed cases.
Results 603 patients were enrolled (199 placebo, 198 Donepezil 5 mg/day, 206 Donepezil 10 mg/day); 425 (70%) had probable VaD and 30% had possible VaD. At Week 24, both Donepezil-treated groups showed significant improvements in cognitive function compared with placebo (ADAS-cog mean change from baseline score effect size: Donepezil 5 mg/day, –1.86, $P=0.002$; Donepezil 10 mg/day, –2.37, $P<0.001$). Donepezil was well tolerated in this population (of whom 89% had co-morbid cardiovascular disease), with low withdrawal rates due to adverse events (placebo, 11.1%; Donepezil 5 mg/day, 11.1%; Donepezil 10 mg/day, 21.8%) and a similar incidence of cardiovascular adverse events across all treatment groups (placebo, 18.1%; Donepezil 5 mg/day, 20.7%; Donepezil 10 mg/day, 20.4%).
Conclusions Donepezil-treated patients with probable or possible VaD demonstrated significant cognitive improvements compared with placebo-treated patients. Donepezil was also well tolerated in this population, which has a high incidence of cardiovascular disease.

P 3113

Donepezil provides cognitive and global benefits in patients with vascular dementia

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Background As evidence suggests that vascular dementia (VaD) is associated with a cholinergic deficit, patients with VaD may benefit from cholinesterase inhibitor therapy.
Objective Evaluation of the efficacy and tolerability of Donepezil in patients with probable or possible VaD.
Design A randomised, double-blind, placebo-controlled, 24-week study (Study 308).
Methods A diagnosis of probable or possible VaD according to NINDS-AIREN criteria was required for inclusion; patients with a prior diagnosis of Alzheimer's disease were excluded. Patients were randomised to receive placebo, Donepezil 5 mg/day or Donepezil 10 mg/day (5 mg/day for first 28 days). Results are reported for intent-to-treat observed cases.
Results 616 patients were enrolled (193 placebo, 208 Donepezil 5 mg/day, 215 Donepezil 10 mg/day); 76% had probable VaD and 24% had possible VaD. Both Donepezil-treated groups showed significant improvements in cognition compared with placebo (ADAS-cog mean change from baseline score effect size at Week 24: Donepezil 5 mg/day, –1.60, $P=0.006$; Donepezil 10 mg/day, –2.12, $P<0.001$). Greater improvements in global function were observed with both Donepezil groups than with the placebo group (% patients showing improvement on the CIBIC-plus at Week 24: placebo, 26%; Donepezil 5 mg/day, 44%, $P=0.006$; Donepezil 10 mg/day, 35%, $P=0.08$; overall treatment $P=0.011$). Donepezil was well tolerated in this population, with low withdrawal rates due to adverse events (placebo, 8.8%; Donepezil 5 mg, 10.1%; Donepezil 10 mg, 16.3%).
Conclusions Donepezil is an efficacious and well-tolerated treatment for patients with probable or possible VaD, and may have an important role in the management of these patients.

P 3114

Donepezil improves cognition both in patients with probable and those with possible vascular dementia

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Background Patients with vascular dementia (VaD) appear to benefit from treatment with cholinesterase inhibitors. However, little is known about the responses to therapy in patients with probable VaD compared with possible VaD.
Objective A comparison of the effects of Donepezil in patients with probable versus those with possible VaD.
Design A combined analysis of two randomised, double-blind, placebo-controlled, 24-week, parallel-group studies (with identical protocols) in patients with probable or possible VaD.
Methods Patients with probable or possible VaD (classified according to NINDS-AIREN criteria) were randomised to receive placebo, Donepezil 5 mg/day, or Donepezil 10 mg/day (5 mg/day for first 28 days). Efficacy measures included the ADAS-cog. Results are reported for week 24 intent-to-treat observed cases.
Results 1219 patients were enrolled; 73% had probable VaD and 27% had possible VaD. In probable VaD patients, significant cognitive improvements compared with placebo were observed in both Donepezil groups (ADAS-cog LS mean change from baseline: placebo, –0.23, n=228; Donepezil 5 mg/day, –1.79, P=0.001, n=235; Donepezil 10 mg/day, –2.91, P<0.001, n=210). Similar results were observed in possible VaD patients (ADAS-cog LS mean change from baseline: placebo, 0.23, n=82; Donepezil 5 mg/day, –2.12, P=0.003, n=82; Donepezil 10 mg/day, –1.17, P=0.07, n=88).
Conclusions Placebo-treated patients with probable VaD maintained levels of cognition over 24 weeks, whereas patients with possible VaD showed minimal decline. Compared with placebo, Donepezil significantly improved cognition both in patients with probable and those with possible VaD, indicating that Donepezil is an effective treatment for the cognitive symptoms of both possible and probable VaD.

P 3115

Benefits of Donepezil treatment in patients with very mild Alzheimer's disease

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Introduction The efficacy and tolerability of Donepezil was evaluated in patients with very mild Alzheimer's disease (AD).
Methods A 24-week, randomised (Donepezil: placebo, 2:1), double-blind study included patients with probable AD (DSM-IV and NINCDS/ADRDA criteria), a mini-mental state examination (MMSE) score of 21–26, and a global clinical dementia rating of 0.5 or 1. Patients received placebo or Donepezil 10 mg/d (5 mg/d for the first 42 days, 10 mg/d thereafter). The Alzheimer's disease assessment scale-cognitive subscale (ADAS-cog) and the MMSE were used to assess treatment-related benefits on cognition. Efficacy analysis was based on the least squares mean change from baseline determined using last observation carried forward analysis of the intent-to-treat population.
Results Baseline demographics, including age, gender, and time to diagnosis, were similar in Donepezil- (n=96) and placebo-treated patients (n=57). Mean (SD) MMSE scores at baseline were 24.3 (1.3) and 24.1 (1.7) for the placebo and Donepezil groups, respectively. ADAS-cog scores were improved from baseline at all visits for Donepezil- compared with placebo-treated patients, with significant treatment differences observed at Weeks 12 (1.9; p=.025) and 24 (2.3; p=.008), and at endpoint (2.3; p<.003). Drug-placebo differences on the MMSE significantly favoured Donepezil at Week 6 (1.4; p=.017), 12 (1.2; p=.035), and 24 (1.4; p=.030), and at endpoint (1.8; p=.002). Withdrawal due to adverse events was low (placebo, 8.8%; Donepezil, 15.6%).
Conclusion: Donepezil treatment improved cognition and was well tolerated in patients with very mild AD. These results further support initiating Donepezil therapy early in the disease course.

P 3116

Sustained Donepezil treatment is associated with lower healthcare costs and utilization in community-dwelling patients with Alzheimer's disease

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Introduction The impact of Donepezil therapy on healthcare costs associated with Alzheimer's disease (AD) in a large population of community-dwelling elderly individuals was evaluated.
Methods A retrospective case-control analysis was conducted on 204 AD patients with prescriptions for Donepezil and 12 or more months of enrolment in a Medicare-managed care organization (MCO) following the date of the first prescription. A control group of 204 patients with 12 or more months of plan enrolment following the diagnosis of AD was selected. Healthcare costs were calculated for cases and controls during the 12-month follow-up period, adjusting for age, gender, comorbid conditions, and complications of dementia.
Results Annual adjusted costs for medical services and prescription drugs were $3891 lower for patients taking Donepezil compared with controls. Adjusted costs were $4192 lower for patients on longer-term therapy (270 or more days supply of Donepezil) and $3579 lower for patients on shorter-term therapy (less than 270 days supply) when compared with controls. Reduced inpatient costs were responsible for 74% of these savings.
Conclusion Donepezil was associated with a significant reduction in costs for patients with AD in this community-dwelling population. Patients receiving longer-term Donepezil therapy incurred the lowest costs, largely attributable to differences in utilization of inpatient services. The lower healthcare costs associated with Donepezil therapy are likely to be the result of improved cognitive functioning and associated improvements in medical management of co-morbidities and complications associated with AD.
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P 3117

Galantamine, a novel drug with unique dual mode of action reduces depression in Alzheimer's disease

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Introduction Galantamine, a novel treatment for Alzheimer's disease (AD) is an allosteric modulator of the nicotinic acetylcholine receptors. A multicenter clinical trial recently performed in Germany investigated the potential influence of nicotinic stimulation on other neurotransmitter systems such as serotonin. The efficacy of galantamine in AD patients with behavioural and psychological disturbances was investigated with a focus on depression.
Methods 245 patients with predominantly mild AD were eligible to receive galantamine 16mg/day or 24mg/day over 6 months. The Neuropsychiatric Inventory (NPI) and "test for early detection of dementia with distinction from depression" have assessed depression (TFDD). The NPI evaluates non-cognitive symptoms including depression. A cut-off >4 points (frequency x severity) was judged for relevant depressive symptoms. Using the TFDD, depression is judged by the physician and in addition by the patient on an 11- item numerical rating scale from "0" (not at all depressed) to "10" (severest depression imaginable). More than 8 points of combined physicians' + patients' evaluation indicate a relevant depressive disturbance. The TFDD correlates with the Geriatric Depression Scale (r=0.73).
Results The NPI depression score (ITT) showed 63% less depressive patients (N=10) after 6 months galantamine treatment versus baseline (N=27). Comparable results emerged from the TFDD: from 41 patients with baseline depression (17.1% of total study population) only 19 patients were still above 8 points at month 6 demonstrating a mean reduction of 54% in depressive symptoms.
Conclusion In this patient population with mild AD, it could be demonstrated for the first time that galantamine has an impact on depression. The substantial reduction in depressive symptoms may indicate that galantamine provides an antidepressive efficacy possibly mediated by serotonin.

P 3118

Galantamine reduces behavioural and psychological disturbances and related caregiver burden in Alzheimer's disease patients

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Background Up to 90% of all Alzheimer's disease (AD) patients develop behavioural and psychological disturbances often escalating in the patient's institutionalisation and the need for caregiver's treatment, respectively. Galantamine (Reminyl®), a novel cholinergic treatment with a unique dual mode of action may delay the onset or improve these non-cognitive symptoms.
Objective To evaluate Galantamine treatment for behavioural disturbances, psychological symptoms, and associated caregiver distress in community dwelling AD patients.
Methods In a 3-month, open-label, Swiss multicenter Phase IV study mild-to-moderate AD patients were treated with galantamine up to 24mg (bid.). The efficacy was assessed upon completed 3-month treatment (observed cases [OC]) with the Neuropsychiatric Inventory (NPI) for primary outcome, the Clinical Global Impression (CGI) for secondary outcome, safety and tolerability monitoring.
Results From 124 patients (mean age 75.2 years, 55.6% women) receiving galantamine (intention-to-treat safety analysis), 91 patients completed the study per protocol (OC efficacy analysis) demonstrating significant improvements in NPI versus baseline (p=0.004) with mean total NPI scores (±SE) reduced from 14.93 (±1.17) to 11.25 (±1.16) after 3 months. Eleven out of 12 NPI domains were improved, the most frequent and severe symptoms being irritability, apathy, depression, agitation, and anxiety improved by 19–38%. The total NPI caregiver burden was significantly reduced at Month 3 (p=0.004) and according to CGI ratings eighty-eight percent of all patients improved or were unchanged. There were mostly gastrointestinal adverse events.
Conclusion In this general clinical setting Galantamine treatment was well tolerated, significantly improved the behavioural disturbances and reduced the behaviour-related caregiver burden.

P 3119

Effect of Donepezil on EEG spectral analysis in Alzheimer's disease

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Introduction EEG spectral analysis (EEG-SA) allows a detailed and quantitative analysis of waveform changes in Alzheimer's disease (AD). Although there have been studies investigating the correlation of EEG-SA and clinical findings in AD, the effect of treatment with anticholinesterase drugs on EEG findings has not been investigated so far.
Material & Methods Eighteen patients with AD entered the study. All patients were given Donepezil 5 mg/day and after 2 months 10 mg/day. Folstein Mini Mental State Examination (MMSE) and EEG's were obtained at baseline and at the end of the 2nd and 6th month. EEG-SA evaluations were done in temporal and centro parietal derivations.
Results Pre-treatment MMSE scores were 16.28±5.03. At the end of the 6th Month MMSE scores increased to 17.87±7.36 but this difference was not significant. Delta amplitudes were reduced and amplitudes in all other frequency ranges increased (p<0.005) in the temporal derivations. In the centroparietal derivations tetha, alpha and beta amplitudes increased (p<0.005) but delta amplitudes remained unchanged. Tetha amplitudes increased in both derivations (p<0.005).
Conclusion We have shown that in AD treatment with Donepezil led to some improvement in cognitive functions and caused a positive effect by decreasing delta amplitudes and increasing alpha and beta amplitudes in EEG-SA. Tetha amplitudes increased despite treatment.
This is the first study investigating the effect of cholinergic treatment on EEG-SA in AD. Our results support other studies showing a modulator role of the cholinergic system on EEG and point to the utility of EEG-SA in the follow-up of treatment in AD.

P 3120

Changes of quantitative EEG after Donepezil treatment in Alzheimer's disease

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Introduction Though symptomatic improvements after treatment of Donepezil is well documented in Alzheimer's disease (AD), the electrophysiological change have not yet been elucidated. Among the parameters of quantitative electroencephalography (q-EEG), high frequency activity, especially gamma rhythm, may play a role in normal cognitive function including the integration of sensory processing, association, coupling or selective attention, which are characteristically impaired in AD.
Methods In order to define the profile of q-EEG changes including gamma rhythm after Donepezil treatment, we followed 17 AD patients for 12 weeks. We analysed the spectra power taken from 16 derivations by averaging twenty-2-sec epoch in normal controls and AD patients. After logarithmic transformation of spectra power, statistical test was done and the effect of Donepezil treatment on q-EEG profile was analysed during follow up period.
Results Before medication of Donepezil, AD patients had a significantly lower alpha spectra power as well as a significant higher delta spectra power, compared with normal control. After medication of Donepezil in AD patients, compared to base-line q-EEG, gamma spectra power was significantly increased, whereas theta spectra power was significantly reduced. Compared to absolute power, relative power was more sensitive in detecting change of EEG after Donepezil treatment
Conclusions This study suggests that Donepezil significantly change theta and gamma spectra power in q-EEG, and the increase in gamma rhythm may be correlated with the clinical improvements after Donepezil treatment.

P 3121

Donepezil in dementia with Lewy bodies

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The objective of this six-month, open-label, prospective study was to assess the clinical efficacy of Donepezil in dementia with Lewy Bodies (LBD). LBD is characterized by cognitive decline with fluctuating course, visual hallucinations and other psychotic manifestations, and parkinsonism.
Method 19 patients with LBD – diagnosed according to McKeith et al (1996) diagnostic criteria – 8 male and 11 female, of 76.3 years mean age, were treated with Donepezil, 5 mg per day, dose which could be increased to 10 mg per day after the first month. Most patients were under concomitant medication. Efficacy of Donepezil was assessed using the MMSE for cognitive performance, the NPI for neuropsychiatric symptomatology and the UPDRS for parkinsonism, at baseline and at the end of the 1st, 3rd and 6th month.
Pre- and post-treatment mean scores for all scales were compared using paired t-test.
Results By the end of the 6th month the MMSE mean 1.4 points raised score and the NPI total score was reduced by 26% ($p<0.01$). Reduction in mean scores for separate NPI items was: for hallucinations 57%, for delusions 48%, for agitation 41%, for apathy 59%. Parkinsonian symptomatology improved slightly.
Medication was generally well tolerated.
Conclusion Donepezil seems to be a safe and effective alternative treatment for LBD, significantly improving cognition, psychotic and behavioural symptoms. The degree of improvement noted in our study was similar to that seen with neuroleptics, a class of medications by definition problematic in LBD due to poor tolerability.

P 3122

Donepezil is well tolerated in patients with vascular dementia: a comparison of tolerability in vascular dementia patients and Alzheimer's disease patients

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Background Donepezil is an effective and well-tolerated treatment in Alzheimer's disease (AD) patients. Donepezil is also effective in vascular dementia (VaD) patients. However, VaD patients have high levels of co-morbid disease and their tolerability profile may therefore differ from that of AD patients.
Objective A comparison of the tolerability of Donepezil 5 and 10 mg/day in patients with VaD and patients with AD enrolled in randomised, double-blind, placebo-controlled trials.
Methods Incidences of adverse events (AEs) across placebo and Donepezil 5 and 10 mg/day groups were compared using data from two 24-week studies in patients with probable or possible VaD, and similar studies in patients with AD.
Results The proportions of VaD patients with AEs were: Donepezil 10 mg/day, 93% (n=421); Donepezil 5 mg/day, 90% (n=406); and placebo, 88% (n=392). The equivalent figures in AD patients were: Donepezil 10 mg/day, 83% (n=642); Donepezil 5 mg/day, 65% (n=821); and placebo, 62% (n=874). The majority of AEs in both VaD and AD patients were of mild intensity. Withdrawals due to AEs were low: 19% and 11% from the VaD Donepezil 10 and 5 mg/day groups, 10% from the VaD placebo group; 14% and 6% from the AD Donepezil 10 mg/day and 5 mg/day groups, 6% from the AD placebo group.
Conclusions VaD placebo- and donepezil-treated groups showed a higher incidence of AEs than corresponding AD groups, indicating that VaD patients are generally "sicker" than AD patients. However, these results nevertheless demonstrate that Donepezil is well tolerated in VaD and AD patients.

P 3123

Greater improvement in cognition and activities of daily living with Donepezil compared to Galantamine in a direct head to head trial in Alzheimer patients

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Introduction Although Donepezil and Galantamine have been studied previously in clinical trials, no direct comparison of these agents in the same trial population has been reported to date.
Methods Patients with mild to moderate AD were randomised to open-label Donepezil (up to 10 mg qd) or Galantamine (up to 12 mg bid) for 12 weeks, according to product labelling. Primary study objectives were to assess tolerability and physicians and caregivers satisfaction with treatment (reported in accompanying abstract). Secondary assessments explored

effects of treatment on cognition using the ADAS-cog (modified 13-item) and the MMSE, and on Activities of Daily Living (ADL) using the Disability Assessment for Dementia (DAD). Trained independent raters blinded to study treatment and adverse events assessed the cognitive measures.
Results A total of 120 patients were enrolled from 4 countries. 64 patients were treated with Donepezil (mean age =73.8, mean baseline MMSE±SD=18.3±3.3) 56 patients with Galantamine (mean age =75.1, mean baseline MMSE±SD=18.4±3.7). Significantly, greater improvements in cognition and ADL were observed for Donepezil compared with Galantamine for the MMSE at endpoint (Week 12 LOCF); for the 13-item modified ADAS-cog at both Week 12 and endpoint; and the DAD at Weeks 4, 12 and endpoint (all P-values <0.05).
Conclusions Cognitive and ADL assessments revealed greater improvement for patients treated with Donepezil compared with Galantamine. In contrast to Donepezil, the necessity of having to titrate Galantamine to a therapeutic dose may contribute to these results.

P 3124

Donepezil compared to Galantamine in Alzheimer's disease: Better physician and caregiver satisfaction/ease of use ratings in a multinational randomised trial

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Introduction Donepezil and Galantamine have been evaluated previously in clinical trials but no direct comparison of these two cholinesterase inhibitors in the same trial has been reported to date.
Methods Patients with mild to moderate AD were randomised to open-label Donepezil (up to 10 mg qd) or Galantamine (up to 12 mg bid) for 12 weeks according to approved product labelling. Tolerability was assessed by reporting of adverse events (AEs). Physicians and caregivers completed questionnaires to rate satisfaction with treatment and ease of use of the medication in daily practice.
Results 120 patients were enrolled from 4 countries. 64 patients were treated with Donepezil (mean age=73.8, mean baseline MMSE±SD=18.3±3.3); 56 patients were treated with Galantamine (mean age=75.1, mean baseline MMSE±SD=18.4±3.7). Both treatments were well tolerated, but a greater proportion of patients receiving Galantamine (46.4%) reported gastrointestinal AEs compared with Donepezil (25.0%). Six (9.4%) Donepezil-treated and 12 (21.4%) Galantamine-treated patients reduced their dose or discontinued treatment temporarily due to AEs. Both physicians and caregivers reported significantly higher total satisfaction/ease of use scores with Donepezil compared with Galantamine at Weeks 4 and 12 and at study endpoint (Week 12 LOCF) (all P-values <0.05).
Conclusions Both treatments were well tolerated, with more gastrointestinal AEs reported for Galantamine compared with Donepezil. Physician and caregiver total ease of use/satisfaction scores were significantly better for Donepezil versus Galantamine in the first reported head-to-head study of these two agents.

P 3125

Effects of Cerebrolysin on brain bioelectrical activity and cognition in humans

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Effects of Cerebrolysin, a peptide preparation with potential neurotrophic activity, on brain bioelectrical activity and on cognitive performance were investigated in neurorehabilitation patients with traumatic brain injury (TBI), in senile dementia patients (SD) and in healthy elderly subjects. TBI and SD patients received repeated i.v. Injections (30 ml/day; 20 infusions/4 weeks) of Cerebrolysin, while a single oral dose (30 ml) of the Cerebrolysin solution were administered to control subjects.
Cerebrolysin increased average alpha activity ($p<0.05$ in O1 and P3 electrodes of TBI patients) and induced a generalized decrease in slow delta activity ($p<0.05$ in F7 and P3 electrodes of TBI and SD patients). In elderly controls, Cerebrolysin also increased alpha activity ($p<0.05$ in O1 electrode) and decreased slow delta activity from 1 to 6 hours after drug intake. Cerebrolysin improved cognitive performance scores with respect to baseline values in SD (MMSE, $p<0.05$; ADAS, $p<0.05$), TBI (SKT reversal naming, $p<0.05$) and control subjects (ADAS memory items, $p<0.01$).
Our results indicate that Cerebrolysin might be a useful neuroprotective treatment in patients with brain damage of traumatic or degenerative cause and in elderly people with age-associated memory impairment.

P 3126

Galantamine improves behavioural disorders and reduces caregiver distress in patients with mild-to-moderate Alzheimer's disease

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Background Controlled clinical trials with Galantamine in over 3200 Alzheimer's disease (AD) patients have demonstrated its broad range of efficacy and tolerability. We investigated the efficacy and safety of Galantamine and its potential to reduce caregiver distress in an ambulant setting.
Methods Patients with mild-to-moderate AD receiving at least one dose of Galantamine were included in the analyses. Dose titration ranged from 8mg/day to 16mg/day or 24mg/day. The 6-month treatment outcome vs. baseline was assessed by Alzheimer's disease Assessment Scale (ADAS-cog-11), Neuropsychiatric Inventory (NPI), physicians Clinical Global Impression (CGI), and General Health Questionnaire (GHQ, evaluating caregivers' emotional distress).
Results 149/245 patients in this open-label trial (mean age 72 years, 59% female, 92% "mild" AD) responded with significant improvements in cognition at month 6 versus baseline (ADAS-cog $_{\text{baseline}}$=24, mean change –1.9, $p\leq0.001$). Almost 1/4 of all patients improved their mean ADAS-cogs by –10.2 points. NPI scores demonstrated significant improvements from week 12 ($p\leq0.01$) with 69% responders at month 6, although the patients entered with very low baseline scores (mean 9.9, severity x

frequency). The decrease in behavioural symptoms corresponded with a significant reduction in caregiver distress (mean −0.5, $p \leq 0.05$). GHQ significantly improved from week 12 ($p \leq 0.001$) onward. At month 6, the caregivers' distress was significantly reduced by 27%. The responder rate was 78%. The CGI showed 65% patients improved after 12 weeks and 83% were improved or unchanged after 6 months. Galantamine was well tolerated.

Conclusion Galantamine demonstrated significant benefits on cognition, behavioural symptoms, and caregiver distress also in mild AD and may thereby be favourable for both, patients and caregivers even in the early stages of the disease.

P 3127

Front temporal dementia with motor neuron disease: A case report with fasciculation's and no bulbar palsy after five years onset.

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Introduction Dementia with motor neuron disease (MND) has been described as a new clinic pathologic entity, characterized by profound breakdown in personality and social conduct, a dynamic spontaneous speech, higher cortical function impairment and clinical manifestations of MND. Pick's disease, frontal lobe degeneration and front temporal dementia with MND consist of the three subtypes of frontal dementia.

Methods/Results We studied a 60 years old male, hospitalised in the Psychiatric Department, five years after the onset of the disease. Patient's clinical spectrum included psychomotor retardation, behavioural disorders, aggressiveness, poor verbal fluency and severe memory and orientation disorder. Primitive reflexes and fasciculation's on biceps and deltoids were noted during physical examination.

Routine blood tests, B 12, folic acid, homocysteine, thyroid hormones and EEG were normal. Brain MRI showed prominent front temporal atrophy. EMG showed neurogenous diagram with fasciculation.

Conclusion Front temporal dementia with MND is a rare disease characterized by presenile onset and 2–3 years survival. In our patient clinical and laboratory studies advocate for the above diagnosis. The specific feature is the long duration of the illness and the lack of bulbar or other manifestations of MND with the exception of fasciculation's. A few reports exist in the world bibliography and furthermore investigation is required in order to determine specific criteria for a secure diagnosis.

P 3128

Therapeutic efficacy of Nootropil on cognitive disturbances in patients with chronic ischemic cerebrovascular disease (CICVD)

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P 3129

Exercise and dementia

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Movement disorders 2

P 3130

Clinical analysis of spinocerebellar ataxia type 2 in Serbian population

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The spinocerebellar ataxia type 2 (SCA2) is dominantly inherited neurodegenerative disease that is characterized with slowly progressive cerebellar ataxia, slow saccades and decreased tendon reflexes. The affected individuals show expanded CAG triplet repeats in ataxin-2 gene, and there is still some controversy about variability of phenotype. The 52 families with autosomal dominant ataxia (ADCA) and 70 isolated cases with idiopathic late-onset cerebellar ataxia from Serbia were analysed for this mutation. Eight affected individuals and one presymptomatic female from 5 families, heterozygous for CAG repeat expansion in the SCA2 gene containing 42–48 repeats, whereas the normal alleles carried 22–23 repeats. We observed a statistically significant inverse correlation between the age of disease onset and the number of CAG repeat units in the expanded alleles (Spearman's correlation coefficient, $p<0.05$). All patients showed gait and limb ataxia, 75% had slowed saccades, 87.5% showed decreased or absent tendon reflexes while only one patient had hyperreflexia. Frequencies of slow eye movement correlated significantly with duration of the disease ($r=0.855$, $p<0.01$). Nerve conduction studies were performed in seven patients, and six of them had sensory dominant axonal polyneuropathy with reduced sensory action potentials. MRI was performed in eight patients. In Serbian population SCA2 mutation accounted for 9.6% of the known Serbian families with ADCA. Our results suggest that the clinical and genetic characteristics of the Serbian families with SCA2 are similar to descriptions of this disease in other populations.

P 3131

DYT1 mutation in primary torsion dystonia in a Serbian population

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Introduction Primary torsion dystonia (PTD) is a clinically and genetically heterogeneous movement disorder. A GAG deletion at position 946 in the DYT1 gene is responsible for most cases of autosomal dominant early-onset PTD.

Methods We analysed the DYT1 mutation in 52 patients from a Serbian population, selected according to the proposed guidelines for diagnostic testing: (a) 39 patients with PTD onset <26 years, and (b) 13 patients with the disease onset >26 years, but with at least one affected family member with early-onset dystonia.

Results and Discussion Five (10%) apparently sporadic patients were positive for the GAG deletion in the DYT1 gene: two with typical, generalized dystonia, one with long-lasting, non-progressive segmental dystonia, one with multifocal, and one with late-onset, jerky axial dystonia. Molecular analysis of relatives in 2 families revealed that the lack of family history was due to reduced penetrance.

P 3132

Bilateral changes in somatotopy of sensorimotor interactions in focal hand dystonia

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Introduction The aim was to detect abnormalities of sensorimotor interactions and their topographic distribution in dystonic patients.
Methods We investigated the effect of digital electrical stimulation on the amplitude of motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (TES) in hand muscles on the affected and unaffected sides of 8 focal hand dystonia patients and 10 age-matched controls. Non-painful digital stimulation was applied to a contiguous finger (CF) and to a non-contiguous finger (NCF), and preceded TMS or TES at intervals from 10 to 100 msec.
Results In normal subjects, a somatotopic inhibitory effect was detected, i.e. CF stimulation provoked a significantly higher MEP inhibition at intervals of 20–50 msec. In dystonic patients, at the same intervals, the digital conditioning resulted in the absence (80% of muscles examined) or inversion (20% of muscles) of somatotopy. These abnormalities were present on both the affected and unaffected hands. TES conditioning provoked MEP inhibition only at ISIs < 40 msec.
Conclusion MEP suppression in response to digital stimulation is preserved in dystonia, but the somatotopic distribution of the sensorimotor interactions is lost or even reversed in dystonic patients. These abnormalities are present at both the spinal and cortical levels. These alterations are similar to the changes in the arrangement of sensory maps, documented in dystonic patients, suggesting a link between sensory abnormalities and the genesis of motor symptoms. Abnormal spatial distribution of surrounding inhibition may account for the altered topography of sensorimotor interactions in dystonic patients.

P 3133

Minocycline as neuroprotection in Huntington's disease

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Objective Huntington's disease (HD) is a relentlessly progressive, incurable autosomal dominant neurodegenerative disorder. Minocycline delayed disease progression in the transgenic mouse model of HD, inhibited caspase-1 and caspase-3 mRNA upregulation, and decreased inducible nitric oxide synthetase activity in the R6/2 model. Survival was extended by 14%.
Methods In an open label study, minocycline was administrated to 18 patients with genetically confirmed HD. The patients were evaluated at baseline, after 2 weeks, and after 6 months of treatment using the motor scale of Unified HD Rating Scale (UHDRS-I).
Results The 14 compliant patients improved in most parts of the UHDRS, including fine motor tasks, whereas four noncompliant patients deteriorated as expected. In all, UHDRS did not change in the first 2 weeks of treatment but improved thereafter to a significant degree in the compliant group. No adverse effects were reported by the patents spontaneously or were observed directly by the investigators.
Discussion This is the first study of minocycline in HD. Whereas prior studies with other potential neuroprotective agents did not show ameliorative effect, we could demonstrate considerable clinical amelioration of symptoms in HD as seen in the animal model. A possible placebo effect is unlikely due to the unchanged motor functions after 14 days. However, our results should be taken with caution due to the open label design but may lead to some hope in this untreatable neuropsychiatric disease.
Conclusion A double-blind, placebo-controlled trial appears highly warranted to definitively establish the value of minocycline in HD.

P 3134

Huntington's disease in Argentina

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Introduction Huntington's disease (HD) is a worldwide neurodegenerative disorder. In South America, large kindred's have been identified in Maracaibo, Venezuela and in Cañete, Perú. To our knowledge no previous studies, have been reported from Argentinean populations.
Objective to describe the clinical and allelic characteristics in 36 Argentinean individuals.
Methods Since 1999, 21 patients with HD, and 15 *persons at risk* from 18 putative HD families were evaluated at the Buenos Aires University Hospital. Clinical findings, age at onset, paternal inheritance and ethnic origin were investigated. They were tested for CAG expanded trinucleotide.
Results Twenty-one women and 15 men were included. Initial symptoms were motor in 45% and psychiatric in 45%, while seizures was the symptom of presentation in 10% of cases. Juvenile onset occurred in 13%. Inheritance was maternal in 50%, paternal in 40% of cases, while in 10% it could not be determined. Expanded alleles varied from 40 to 85 CAG units in affected individuals while normal alleles varied from 11 to 33 CAGs. In 10/15 *persons at risk;* CAG expansion was positive in 3 and negative in 7 individuals. Paternal inheritance was linked to greater increases in repeat size. Ethnic distribution included 18 families; 6 European – Latinos, 5 Saxons, 3 Hispanics (Bolivia, Paraguay and Argentina), and 1 from Syria, in three cases data were not available.
Conclusion Comparing European and Argentinean HD populations of European descent could be of interest to disclose the role of environmental factors in the phenotype expression of HD.

P 3135

Development and validation of the Restless Legs Syndrome Quality of Life Questionnaire

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Introduction Restless Legs Syndrome (RLS) is a neurological, sensorimotor disorder in which a person experiences a strong urge to move the legs or other extremities while at rest, severely impacting sleep and daily life. No questionnaires currently exist

to assess this impact on daily life, however. The objective was to develop and validate an RLS-specific quality of life (QoL) questionnaire (RLSQoL).
Methods The 18-item RLSQoL was developed from clinician- and patient-centred item generation to assess the impact of RLS on daily life, concentration, sex life and work life. The RLSQoL was administered twice over a 2-week period to 85 adults with primary RLS. Using a patient-reported version of the RLS Rating Scale (RLSRS-PV), patients rated the severity of their symptoms and whether these symptoms changed over the 2-week period. Analyses were performed to assess reliability, validity and preliminary responsiveness.
Results The RLSQoL yielded a summary score with a range of 0–100; higher scores indicated better QoL or less life impact. This summary score demonstrated good internal consistency reliability (alpha >=0.93), test-retest reliability (intra-class correlation coefficient >=0.84) and item-convergent validity (item-scale correlations >=0.40). The RLSQoL distinguished between groups with differing RLSRS-PV symptom severity ($F=50.55$, $p<0.0001$) and was sensitive to even rather small changes in RLS status over a 2-week period using patient reports of symptom change.
Conclusions The RLSQoL is a valid and reliable measure of the impact of RLS on patient QoL and is sensitive to short-term changes in RLS severity.

P 3136

The Impact of Restless Legs Syndrome (RLS) on Quality of Life (QoL)

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Introduction There is support for the view that RLS is a CNS dysfunction involving dopaminergic pathways. Sufferers experience sleep loss, extreme discomfort and disruption of normal activities. Assessment of the burden of RLS is critical for evaluating its clinical significance and treatment benefits but its impact on QoL is currently unknown. This study assesses that impact compared with a normative population (norms).
Methods The Short Form 36 (SF-36) was administered to 85 patients with primary RLS referred to a specialist clinic. Scores from this group were compared with published norms for SF-36 scales.
Results The majority (64.5%) of patients were women; the mean (±SD) age was 62.4 (±14.0) years; 67.1% of patients reported experiencing RLS symptoms almost daily. Significant deficits (10–40 points on 100-point scales) in physical functioning, bodily pain, role functioning, mental health, general health and vitality were noted for the RLS group compared with norms, even when examining results by gender and age. Only those RLS patients over 75 years of age had better scores than age-matched peers (who were experiencing one or more other conditions). In general, scores for RLS patients were equivalent to or worse than scores for norms with depression, arthritis, hypertension or cardiac problems.
Conclusion These results suggest a significant impact of RLS on QoL that matches or exceeds that for other major medical disorders. This should be considered when evaluating treatment needs for RLS. Research using larger sample sizes over longer periods of time will examine further the impact on QoL.

P 3137

Cabergoline in RLS – a double-blind, placebo-controlled, multicentre dose-finding trial

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Introduction Cabergoline is a dopamine agonist (DA) with a long elimination half life (>65 hours) that has shown efficacy in preliminary studies in RLS patients. DAs may possess therapeutic properties superior to levodopa in RLS. This study assessed the efficacy and minimum effective dose of cabergoline in RLS patients in a randomised, double-blind, placebo-controlled multicentre dose-finding parallel group study.
Methods 86 Patients with moderate to severe RLS were stratified into 4 treatment groups receiving a target dose of 0mg (placebo), 0.5mg, 1mg and 2mg cabergoline once in the evening. Primary endpoint was the reduction of RLS severity at night between baseline and week 5 (scale 0 to 10).
Results All 3 cabergoline treatment groups showed a clinical improvement of (1) the RLS severity at night compared with baseline in contrast to placebo; statistical comparison showed highly significant differences for all 3 cabergoline doses versus placebo. Similar results have been found for (2) the RLS severity before bedtime, (3) RLS severity at day, (4) overall RLS severity in the IRLSSG rating scale, and (5) satisfaction with sleep. The number of adverse events (AEs) with possible relationship to the study drug were placebo: 54.5%, 0.5mg: 66.7%, 1mg: 55%, and 2mg: 59.1%. No serious AEs occurred.
Conclusions Cabergoline is a highly efficacious drug for RLS patients. All tested doses (0.5mg, 1mg, and 2mg) were effective compared to placebo. The higher dose provided better effects on daytime symptoms than lower doses of drug compared to placebo.

P 3138

Augmentation of the restless legs syndrome in relation to long-term treatment with pramipexole and cabergoline

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Introduction RLS patients treated with dopamine agonists can develop augmentation. In a recent study with pramipexole, augmentation occurred in only 5 of 60 RLS patients treated for ≥6 months. In this study, 118 RLS patients treated with pramipexole or cabergoline show these agents can successfully reduce or eliminate augmentation.
Methods Open-label study in RLS patients administered pramipexole or cabergoline for ≥6 months. *Pramipexole:* 102 patients (mean age =56 yrs; mean RLS duration =26 yrs; primary form =78; secondary =24); doses: 0.25, 0.5, 1.0 mg (in 68, 18, 16 patients, respectively). *Cabergoline:* 16 patients (mean age =58y; mean RLS duration =18 yrs; primary form =16); doses: 0.5, 1, and 2 mg (in 3, 12, and 1 patient(s), respectively). (All received a single dose 2h before bedtime). Seventy-two patients previously received clonazepam (39), gabapentin (23), levodopa (1), pergolide (17), or other (33). RLS diagnosis was made according to ICSD criteria; nocturnal PSG showed PLMS in all patients.
Results Pramipexole-RLS augmentation observed in 9 patients (doses =0.25, 0.5, 1.0 mg (in 6, 2, and 1 patient(s), respectively) after 4, 8, 12, and 15 weeks (in 2, 4, 2, and 1 patient(s), respectively). Previously drugs: clonazepam (4), pergolide (2), pramipexole (1), or opioids (1). Cabergoline- No patients presented augmentation.

Conclusion Cabergoline produced no augmentation. With pramipexole, RLS augmentation occurrence was low (8.3%), unrelated to dose, occurred within 4 months of treatment, and more frequent in secondary than idiopathic RLS (p=.03, Fisher test). Pramipexole and cabergoline may be used to reduce or eliminate augmentation in patients with RLS.

P 3139

Hemifacial spasm: a clinical and epidemiological study in 52 patients

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Objective Hemifacial spasm (HFS) is a peripheral focal myoclonus characterized by unilateral and intermittent spasms in the muscles innervated by the facial nerve. Several reports suggest that primary HFS and arterial hypertension may coexist. We conducted a case–control study to determine whether hypertension occurs more frequently among HFS patients than normal controls.
Materials and methods Cases were selected during a 6-year period among consecutive patients attending one neurological institution. Information was obtained by a standardized questionnaire administered by a trained medical interviewer. Collected data included age, sex, HFS duration, time range between the first symptoms and the correct diagnosis of HFS, education, cigarette smoking, and history of hypertension. We corrected for a bias in case selection by designing a single-centre investigation, recruiting all the consecutive patients who met the eligibility criteria during the study period and using normal controls from the general population of the same area.
Results Primary HFS was diagnosed in 52 subjects (22 men and 30 women, age 63.1±12.5 years) according to published criteria. Mean disease duration was 6.7±11.6 years. HFS was left sided in 30 case patients and right sided in 22. CT or MRI of the brain excluded secondary causes in all patients. The association between exposure variables and case–control status was examined in univariate and multivariate conditional regression models. Hypertension was observed in 22 case subjects and 29 controls (OR=0.55, IC 95% 0.23–1.35).
Discussion Our case-control study does not suggest an association between hypertension and HFS. Further studies are needed to better elucidate this relationship.

P 3140

International database of Tourette syndrome: pilot project in the Czech Republic

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Tourette syndrome (TS) is a neuropsychiatric disorder characterized by multiple motor and vocal tics and accompanied with behavioural disorders. The international database of TS involves 3500 patients from 22 countries (1). Since 2001, the Movement Disorders Centre of General Faculty Hospital, Prague participates in the project. Czech translation of the original form is used. The patients are diagnosed according to the criteria of Tourette Syndrome Study Group. Until April 2002, 50 individuals (36 male and 14 female) have been included. Their average age was 21.9 years (from 9 to 76). Average age at tic onset was 7.7 years (2–19). The age at diagnosis of TS amounted to 16.2 years (5–50), the delay in diagnosis was 8.5 years (0–40). Positive family history was present in 21 cases (42% of patients). Abrupt onset or upsurge after infection was reported by 5 patients (12%). 15 patients (30%) had prenatal or perinatal problems. 41 patients (82%) used medication for tics. 8 patients (16%) did not suffer from other symptoms than tics ("TS only"). Attention deficit hyperactivity disorder occurred in 17 patients (34%), obsessive-compulsive disorder in 11 (22%) and self-injurious behaviour in 8 (16%). Our findings do not substantially differ from the original survey. The drawn data provide valuable information on the clinical characteristics of TS and can serve as a source for further genetic, clinical or pharmacological studies.
References
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P 3141

Apolipoprotein E genotypes and phenotypic expression in Wilson's disease

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Wilson's disease (WD) is a disorder of biliary copper excretion that may result in severe neurological symptoms and advanced liver disease. The wide variation of phenotypic disease expression cannot be fully explained by the different mutation of the Wilson disease gene. The apolipoprotein E (APOE) is associated with onset of Alzheimer's disease, and possibly other neurodegenerative disorders. Moreover, in a recent report it was hypothesized that APOE genotype ubiquitously determines the efficacy of neuronal maintenance and repair in these diseases. The aim of the present study was to determine if APOE genotypes are associated with onset age of WD. We studied 59 unrelated patients with WD. An investigation profile was established in which the patients were grouped according to the clinical symptoms at presentation and APOE status. The distribution of ApoE genotypes in our patients did not deviate from known distributions in healthy European subjects. The average age at which neurological features appear is significantly later (p=0.019) than the average age of onset of hepatic WD manifestation (25.4±7.8 vs. 21.4±8.2 years, respectively). Within the group of patients with predominantly neurological form of WD, the onset of symptoms was significantly delayed (p=0.045) in patients with ε3ε3 genotype (27.0±7.8 years) in comparison to patients with the ε3ε4/ε4/ε4 genotype (21.8±7.1 years).
In conclusion, our data suggest that APOE is associated with age at onset of neurological form of WD.

P 3142

Coenzyme Q10 shows neuroprotective effects in mice dopaminergic culture systems

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In Parkinson's disease (PD), the death of dopaminergic mesencephalic neurons is discussed as the consequence of excessive formation of free oxygen radicals due to mitochondrial dysfunction. While Coenzyme Q10 is known as of beneficial value in a

variety of diseases associated with increased oxidative stress, we investigated the protective effects of CoQ10 in primary cultures of mice mesencephala and organotypic striatal cultures.
Non-crystalline nanoparticles containing CoQ10 as a supercooled melt (guttaQuinon TM) were administered to cultured neurons of both culture systems with or without 1-methyl-4-phenylpyridinium (MPP+, 10 microM) treatment. CoQ10 (0.1 nM –100 microM) increased the survival rate of MPP+-damaged dopaminergic neurons by 75% (0.001 microM). With higher concentrations of CoQ10 the survival effect showed a plateau of 50%.
In organotypic striatal cultures an enhanced production of lactate could be measured in the supernatant after administration of MPP+ (10 microM and 1 mM) if compared to control cultures (25% and 55%). Simultaneous treatment with CoQ10 prevented this additional formation of lactate significantly (100% with 10 microM MPP+ and 35% with 1mM MPP+). Additionally, in the striatal cultures, CoQ10 showed beneficial effects concerning various enzymes of the energy metabolism that were damaged by MPP+, and also increased the activity of both, the hexokinase and the tyrosine hydroxylase, respectively.
CoQ10 has the capacity to protect dopaminergic neurons in vitro, and is neuroprotective to cultured neurons that were damaged by MPP+, a substance often used in models of PD.

P 3143

Dopamine receptor agonists mediate neuroprotection in malonate-induced striatal lesion

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Mitochondrial bioenergetic defects are involved in neurological disorders associated with neuronal damage in the striatum, such as Huntington's disease or cerebral ischemia. The striatal release of neurotransmitters, in particular dopamine, may contribute to the development of the neuronal damage. Recent studies have shown that dopamine agonists may exert neuroprotective effects via multiple mechanisms, including modulation of dopamine release from nigrostriatal dopaminergic terminals.
In rats, intrastriatal injection of malonate, a reversible inhibitor of the mitochondrial enzyme succinate dehydrogenase, induces a lesion similar to that observed following focal ischemia or in Huntington's disease. In this study, male Sprague-Dawley rats were injected systemically with increasing concentrations of D_1, D_2, or mixed D_1/D_2 dopamine agonists prior to malonate intrastriatal insult. Rats were sacrificed after three days; brain sections containing the striatum were stained, histochemically, for cytochrome oxidase (COX) activity. The neuroprotective potential of the drugs of interest was assessed by measuring the malonate-induced lesion volume, as expressed by the absence of COX staining. Administration of increasing doses of the D_2-specific agonist quinpirole, resulted in increased protection against malonate toxicity, as measured by a decrease in the lesion volume. Conversely, the D_1-specific agonist, SKF-38393, as well as the mixed D_1/D_2 agonist apomorphine, conferred higher neuroprotection at lower than at higher drug concentration. Our data suggest that malonate-induced striatal toxicity can be attenuated by systemic administration of dopamine agonists, with D_1 and D_2 agonists showing different profiles of efficacy.

P 3144

Ibuprofen has a protective effect in neurodegeneration caused by intoxication with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in mouse.

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Non-steroid anti-inflammatory agents are suggested to have a positive effect in neurodegeneration. In this study we investigated the effect of ibuprofen (IBF) on neuronal survival after intoxication with MPTP. MPTP is a toxin that damages dopaminergic cells of the substantia nigra (SN) and causes a decrease of the dopamine content in striatum.
Methods C57Bl male mice, 5 months old, were intoxicated with MPTP (60mg/kg) and prior to intoxication they received IBF (Sigma) in the doses of 10 and 30 mg/kg i.p. Next they received IBF every day to the 7th day of observation. In order to assess nigrostriatal degeneration the dopamine content in striatum were measured by high-pressure liquid chromatography (HPLC) on the 3rd and 7th day following intoxication.
Results MPTP alone diminished dopamine content in striatum by about 90% on the 3rd and 7th day as compared to control ($p<0.002$). Administration of IBF + MPTP caused statistically lower decrease of dopamine as compare to animals that received only MPTP: by 84% on the 3rd day in both doses of IBF ($p<0.003$) and by 75% ($p<0.01$) and 68% ($p<0.006$) on the 7th day in doses of 10mg/kg and 30mg/kg respectively. IBF alone did not change dopamine level.
Conclusion Our data indicate that IBF have a neuroprotective effect to neurons injured by MPTP intoxication. This effect was greater if the treatment was prolonged to the 7th day and was dose dependent. The mechanism of IBF action however is unclear and may consist of both anti-inflammatory and direct neuroprotective effect.

P 3145

Pro- and anti-inflammatory cytokine mRNA expression in the striatum of C57B1 male mice following intraperitoneal administration of 1-methyl- 4-phenyl-1,2,3,6 tetrahydropiridine (MPTP)

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The inflammatory reaction have been linked with Parkinson's disease (PD). The neuroinflammation is regulated by numerous signal molecules, including cytokines. The increased density of pro-inflammatory cytokine-producing glial cells in the substantia nigra of patients with PD was documented. This may have several implications for the pathophysiology of this disease. Although the possibility that this cytokines have a neuroprotective effect in this conditions cannot be excluded.
With this context, mRNA levels of IL1beta, IL6, TNFalfa, IFNgamma, IL10 were measured by semi-quantitative RT-PCR in the striatum of mice after 6h, 1, 3, 7 and 14 days post MPTP intoxication. MPTP damages the nigrostriatal dopaminergic neurons.

In the control baseline levels of mRNA for the cytokines assayed were minimal. IL1beta, IFNgamma, TNFalfa expression was rapidly increased, already at 6h after MPTP injection and peaking at 6h to 24 h. The expression of TNFalfa and IFNgamma mRNA appears to be biphasic. The second increase of IFNgamma and TNFalfa mRNA was detected at the 7th day after intoxication. IL10 mRNA showed also phasic expression pattern. Two peaks of IL10 mRNA were seen, immediately (6h) and at the 3rd day post MPTP injection. The moderate increase in the level of IL6 mRNA was observed within 1–3 days following MPTP intoxication. The level of mRNA for IL6 peaked at 7th day time point.
Many of cytokines are expressed post MPTP intoxication. These findings suggest that the cytokine network should be studied in detail. The pharmacological modification of the cytokines synthesis may represent a therapeutic intervention that could reduce the neurodegeneration.

P 3146

Nitric oxide synthase mRNA expression and neurotransmitters levels in the striatum of C57Bl/6 mice following toxic degeneration caused by 1-methyl-4-phenyl-1,2,3,6-tetrahydropiridine (MPTP).

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Nitric oxide (NO) is involved in important physiological functions of the CNS, including neurotransmission, memory and synaptic plasticity. Under conditions of excessive NO formation, it can act as a neurotoxin and may have a role in the pathogenesis of neurodegenerative disorders such as Parkinson's disease (PD).
Methods and results In the present study we examined inducible iNOS and neuronal nNOS mRNA expression in the striatum of C57BL/6 male mice post MPTP intoxication. MPTP is a toxin, which selectively damages dopaminergic neurones. The animals were sacrificed at 6 h and on the 1st, 3rd, 7th, 14th day after MPTP intoxication. The levels of mRNA for iNOS and nNOS were assayed by RT-PCR method. In the control baseline levels of mRNA for iNOS were minimal. Its expression rapidly in-creased from the 6h after MPTP injection, lasting to the 14th day. Neuronal NOS mRNA showed increase after 24 h and peaked within 3–14 days following MPTP intoxication. Using HPLC we examined neurotransmitters levels. The significant decrease in the level of DA was observed within 1–14 days following MPTP injection, achieving minimal level within days 3–7. The levels of DOPAC and HVA were minimal at the 3rd day post intoxication. The moderate increases in the level of 5HT and 5HIAA were seen 6h after MPTP injection.
In **conclusion** – NO may be a key mediator of nigral degeneration playing a significant role in MPTP inducing PD model. Therefore, pharmacological regulation of NO synthesis offers an important strategy for treatment of neurodegenerative diseases.

P 3147

Influence of parathyroid hormone on the functional state of the noradrenergic system of the Brain

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The **aim** of our investigation is to reveal the influence of parathyroid hormone (PTH), regulator of calcium metabolism, on functional activity of the locus coeruleus (LC) neurons, from which the ascending dorsal noradrenergic pathways originate and innervate the different parts of the CNS.
The background impulse activity (BA) of the LC neurons of narcotised rats in norm and after intracarotidal PTH injection (in dose of 0.5Un/100g of weight) was studied extracellularly. The experimental data have been analysed by means of a special computer program. It was shown that the PTH injection leads to significant changes of the statistic characteristics of LC impulse activity: mean frequency, the coefficient of variation, the mode of midi pulse intervals distribution, the coefficients of asymmetry and of excess.
Correlation of the midi-pulse intervals distribution histograms, autocorrelograms and the serial correlation coefficients of the activity sample before and after the PTH injection testifies the significant changes of temporary organization of the impulse flows generated by these neurons under the hormone influence. It was revealed the preferably activating influence of PTH on background activity of LC neurons and strengthening of the phonal afferent signals coming to the LC neurons through different heterogeneous inputs. It is also shown the PTH influence correlates with the BA frequency consisting in that the activity of "low-rate" neurons increases, while the activity of "high-rate" neurons, on the contrary, decreases.
In **conclusion**, we have shown the regulatory and modulatory influence of the PTH on functional state of the LC neurons.

P 3148

Recovery after cerebellar lesions in immature rats

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Cerebellar lesions causing severe movement disorders have been described elsewhere. In the present study, discrete lesions either by suction or focal microinjection of kainic acid were produced in different regions of the cerebellar vermis in 20-day-old male and female rats. The degree of lesion and the sensorimotor recovery were compared. Rolling and circular motions noted after lesion of the folia VIII–X and extension of the limbs and other postural changes noted after lesions of the folia II–IV were gradually reduced within 3 weeks. After 3 months, using foot-flick test 80% recovery was noted in most of the animals. After 6 months, excepting 20% of the posterio-cerebellar vermal lesioned rats no appreciable movement disorder was noted in other animals. It was also noted that the overall recovery processes were faster in anterior vermal lesioned animals as compared to those of posterior vermal lesioned animals. Unlikely to my other studies like sexual and feeding behaviour, no remarkable sex difference was noted in this sensorimotor recovery. The morphological basis for this recovery is yet to be explored.

P 3149

Iron and oxidative stress in neurodegeneration

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Neurodegenerative diseases are progressive disorders that affect selected neuronal populations of the central nervous system, the exact pathogenesis of this mechanism being unknown. Oxidative damage may contribute to neurodegeneration and oxidation reactions are influenced by the regional concentrations of transition metals such as iron.
Hallervorden-Spats disease (HSD) is a rare disorder characterized by an over accumulation of iron in the globus pallidus. Progressive Supranuclear Palsy (PSP) is another neurodegenerative disorder where increased levels of iron have been reported in basal ganglia and mesencephalus.
Methods We report ten patients clinically diagnosed as HSD and fifteen patients with a diagnosis of Probable PSP. The activity of antioxidant enzymes gluthathione peroxidase (GLPX) and superoxide dismutase (SOD) was assessed in red blood cells of patients, by a spectrophotometric assay, and compared with healthy controls.
Results A significant increase of SOD activity was observed in HSD patients: 539+/–174.4 U/g Hb and 379.94+/–50.65 U/g Hb for controls. Simultaneous a decrease in GLPX activity was found in both HSD and PSP patients. The GLPX activity was: 9.6+/–2.5 U/g Hb for HSD patients and 12.23+/–1.6 U/g Hb for controls and 6.1+/–2.6 U/g Hb in PSP patients and 9.6+/–2.3 U/g Hb for controls.
Conclusion In the presence of an increase in iron concentration proved to occur in both of this disorders, hydroxyl radical (OH.) is formed according to the Fenton-reaction. Under these conditions oxidative stress is strongly suggested to occur leading to neuronal injury.

P 3150

The role of dopamine agonists in the pharmacotherapy of bipolar depression

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Introduction Reduced dopaminergic activity is associated with idiopathic and bipolar depression, as well as depression in Parkinson's disease (PD). Results with several antidepressants are controversial or poor, with the exception of nortriptyline and bupropion. Attention should be paid to DAs such as pramipexole (PPX), a selective dopamine agonist with selectivity for the D3 receptor, in the treatment of these conditions.
Methods 32 patients were referred with a history of Type I BAD (current episode of Major Depression according to DSM-IV). All patients had received combined anti-depressive treatment for 7 weeks: daily nortriptyline and fluoxetine, with either li-thium, carbamazepine, or sodium valproate. Patients were treated with pramipexole (PPX) 3.125 mg daily for 12 weeks. The HAMD-17 Scale was used for the assessment of depressive symptoms.
Results During the first 3 weeks, there was an 18% reduction in HAMD-17 scores; after 9 weeks, 27%. The mean reduction was 34% in 30 of 32 patients. Of the 30 patients who completed the study, no one had any adverse event. Drop-outs (2) for inefficacy and adverse events (insomnia, dry mouth, hypotension, and vomiting) occurred.
Conclusion The high affinity of PPX for D3 receptors may account for its efficacy in bipolar depression and conditions with psychomotor retardation. The great affinity of pramipexole for D3 receptors is possibly the reason for its efficacy in improving the mood of patients with bipolar depression, as well as conditions with psychomotor retardation such as PD, negative symptoms of schizophrenia, and unipolar depression.

P 3151

Long/term Prognosis of vascular hemiballism

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Background and purpose The information concerning the long-term prognosis of vascular hemiballism (HB) are very limited, although it was formerly thought to have a poor prognosis with inexorable progression to death within weeks or months. The aim of this study was to prospectively evaluate the long-term prognosis of HB due to first-ever ischemic strokes.
Methods A cohort of 27 patients with HB due to first-ever ischemic strokes (mean age, 68 years) was followed for a mean period of 30 months (range: 5 days to 150 months), with 2 patients lost to follow-up. Death and stroke recurrence rates were evaluated by Kaplan-Meier analysis.
Results During the follow-up period there were 11 deaths (44%). The survival rate was 85% (95%CI, 71% to 99%) at 6 months, 81% (95%CI, 65% to 97%) at 15 months, 51% (95%CI, 24% to 78%) at 36 months, and only 32% (95%CI, 4% to 60%) at 150 months. The survival rate free from recurrent stroke was 96% (95%CI, 87% to 100%) at 6 months, 91% (95%CI, 79% to 100%) at 12 months, 80% (95%CI, 61% to 99%) at 24 months, and 27% (95%CI, 0% to 71%) at 150 months.
Conclusions The long-term prognosis of patients with HB due to first-ever ischemic stroke is not specifically determined by the very nature of the clinical manifestation of this rare type of involuntary movements. Instead, their long-term prognosis is similar to that of other stroke patients, i.e. follows the etiological pattern of HB.

P 3152

Olanzapine improves tardive dyskinesia in patients with schizophrenia

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Introduction We report preliminary findings of the effects of olanzapine (OLZ) treatment upon tardive dyskinesia TD.
Methods Eligible schizophrenic subjects met restricted Research Diagnosis Tardive Dyskinesia criteria (restricted RD-TD) that specified for abnormal involuntary movements to be of at least moderate severity. Subjects received OLZ, 5–20 mg/day for 8 months within a double-blind design that included up to 2 medication reduction (75%) periods of 2 weeks duration. TD was assessed with the Abnormal Involuntary Movement Scale (AIMS) and psychopathology with the Positive and Negative Syndrome Scale (PANSS)(c).
Results A significant reduction in mean AIMS Total score was demonstrated (N=95; BL=11.9; EP=7.5; p<.001; LOCF). Nearly 70% of subjects no longer met the restricted RD-TD criteria after up to 8 months of treatment, with greater than 50% improving as early as 8 weeks. No statistically significant

rebound worsening of TD was found during the blinded drug reduction periods. A significant improvement in the PANSS occurred (BL=68.2; EP=59.7; p<.001, LOCF).
Conclusions These data, suggesting an ameliorative, rather than masking effect, and the concurrent further improvement in clinical status suggests that OLZ may offer a potential treatment alternative for managing the schizophrenic patient with pre-existing TD.

P 3153

Friedreich's ataxia associated with agenesis of the corpus callosum: case report of three sisters

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Friedreich's ataxia (FRDA) is an autosomal recessive disorder that usually begins before the age of 20 years and associated with an unstable expansion of a GAA trinucleotide repeat in the first intron of the FRDA gene on chromosome 9q13. Beside classical FRDA, DNA testing confirmed the existence of atypical variance of FRDA amongst which is late onset FRDA with disease onset after the age of 25 years with frequently retained reflexes and less pronounced extra neuronal complications. Agenesis of the corpus callosum is common malformation with the symptoms that may be unrecognised or minimal, or there may be deficit in the interhemispheric transfer of perceptual information for verbal expression. We report three sisters with PCR testing confirmed FRDA and different age of onset. One of the sisters with age of onset before 25 had typical clinical features (ataxia of gait and limbs, loss of vibration sense, muscle weakness and atrophy, loss of deep tendon reflexes, scoliosis and diabetes mellitus) associated with agenesis of the corpus callosum on brain MRI with consecutive displacement and dilatation of the lateral ventricle. The other two sisters had an atypical beginning at the age of 26 and 37 years with similar clinical features but without extra neuronal complications and brain malformation. Despite of different age of onset they had similar number of GAA triplets. We are presenting this family because the probability of inheriting FRDA in three siblings is very low and there is an unusual association with agenesis of corpus callosum.

P 3154

Is Olanzapine the treatment of choice in Huntington's disease?

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Objective The therapy of motor symptoms, especially chorea, in Huntington's disease (HD) is rather difficult. Typical neuroleptics decrease chorea, but care is needed not to increase to doses that impair the individual's functional level.
Methods In our study, olanzapine was administrated to nine patients with genetically confirmed HD in increasing doses until satisfactory clinical effect or the appearance of side effects. The patients were evaluated at baseline and after 14 days of treatment using the motor scale of Unified HD Rating Scale (UHDRS).
Results The patients improved significantly in 5 of 7 subscores of the UHDRS, including oculomotor function, orolingual function, fine motor tasks, chorea, and statics and gait. No adverse effects were reported by the patents spontaneously or were observed directly by the investigator, although some patients needed rather high dose (30mg per day).
Discussion This study could clearly demonstrate that prior studies used the wrong dose. It is worthwhile mentioning the amelioration in those sensitive fields, which's impairment was so far said to be the unavoidable drawback of all neuroleptic medication: oculomotor function, orolingual function, and fine motor tasks. The investigators saw a significant improvement in those motor categories – despite the high doses of olanzapine.
Conclusion High-dose olanzapine seems to be useful in choreatic HD patients. A double-blind, placebo-controlled trial appears highly warranted to definitively establish the symptomatic value of olanzapine in HD.

P 3155

Bone mineral density in Huntington's disease

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Background HD is an autosomal dominantly inherited neurodegenerative disorder due to an increase of CAG repeats in chromosome 4. It is characterised by movement disorder like chorea or gait disability, psychiatric symptoms (depression or psychosis) and dementia. HD patients have an increased risk for falling and perhaps for bone fractures due to their movement impairment.
Design/Methods 15 HD patients (31–73 years) and 100 age and sex-matched controls underwent BMD measurements at the lumbar spine and femoral neck by dual-energy X-ray absorptiometry (DXA, Hologic 4000 plus). Biochemical markers of bone metabolism osteocalcin (OC), c-terminal linked telopeptides of type I collagen (CTX), 25-(OH)-vitamin D, prolactine (PRL) and routine laboratory parameters were assessed.
Results Patients and controls were comparable for anthropometric data and lifestyle factors. Past medical history was evaluated using patients' neuropsychiatric documentation. HD patients had a significantly decreased BMD at the spine as compared to controls (p=0.03). Furthermore, OC and CTX were significantly elevated in HD patients (p=0.0001 and p=0.02, respectively). PRL levels had no statistical effect on BMD so far.
Conclusions HD patients had a significantly decreased BMD and significantly increased bone turnover. This is the first time to describe disturbed bone metabolism and BMD in these patients. Possible causes for these findings may be either an influence of molecular changes due to HD in bone metabolism or the effect of neuroleptic medications in these patients. Our findings indicate that investigation of BMD and bone metabolism is relevant in HD patients due to their high risk for falling.

P 3156

Clinical-pathomorphological correlation in patients with symptomatic dystonias

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Objective To detect the site of lesions in relevant structures by means of magnetic resonance imaging in patients with symptomatic dystonias, to define their clinical characteristics and to

estimate the clinico-morphological correlation between clinical presentation and CNS lesions.
Patients On the basis of performed imaging, there were proved symptoms-correlated lesions in fifty-seven patients with different types of dystonia, according to time of their appearance.
Results Our study included 57 patients with symptomatic dystonia, which appeared as a consequence of focal or multifocal lesions, out of which 7 patients had generalized dystonia, 18 hemidystonia, 6 segmental dystonia, 7 torticollis, 6 blepharospasm, 7 hand dystonia, 3 spasmodic dysphonia and 3 had oromandibular dystonia. Viewed from a highly statistical incidence, stroke was the most frequent cause of structural lesions (33/57 or 57.9%). Relevant pathomorphological changes were present in 50/57 (88%) patients, where 25 (50%) of the patients had lesion in the lenticular nucleus (including individual damage of the putamen and globus pallidus), 12/50 (24%) exhibited thalamus damage and 6/50 (12%) had the damage of the brainstem.
Conclusion Generalized dystonia was most frequently associated with bilateral lesion of the putamen, hemidystonia with lesion of contralateral putamen, torticollis with the damage of the caudate nucleus, hand dystonia with lesion of the thalamus and blepharospasm with lesion of the upper brainstem.

P 3157

Huntington's disease: relation between clinical, genetic and morphometric parameters

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We analysed clinical data in 80 genetically verified patients with Huntington's disease (HD) and measured the severity of the caudate nucleus atrophy in all patients using computed tomography (CT) planimetric assessment. We compared the results with values obtained in 43 age matched healthy subjects. The mean values of caudate nucleus between HD patients and healthy controls were significantly different ($p<0.001$). We found statistically significant inversed correlation between the amount of CAG triplet repeats and the age at the onset of HD ($a<0.001$). We also observed significant inversed correlation between the duration of HD and the progression of the atrophy of the caudate nucleus ($a<0.001$). The natural atrophy of caudate nucleus in healthy controls is also present but without the overlapping of the values obtained in HD patients ($a<0.01$). The amount of CAG triplet repeats in not connected with the character of the first clinical symptoms (motor or psychiatric). Furthermore, the age of the onset of HD is not dependent on the character of the initial symptoms. We observed no relationship between the presence of maternal or paternal heredity and the amount of CAG triplet repeats in HD patients. Moreover, the character of heredity does not influence the age of the onset of HD in our patients. The planimetric measurement of caudate nucleus appeared to be a sensitive tool for the diagnosis of HD.

P 3158

Decreased aconitase activity in Huntington's platelet

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The aetiology of the selective neuronal death that occurs in Huntington's disease (HD) is still unknown despite the identification of a gene with expanded CAG repeats but unknown function. Similar to other neurodegenerative diseases an impairment of oxidative phosphorylation enzyme activities restricted to the basal ganglia in HD brain was found. Especially complex II/III and complex IV were found decreased. Recently decreased aconitase activities were observed in basal ganglia whereas enzyme activities in other brain regions and fibroblasts remain unchanged. Decreased aconitase activity was connected with increased oxidative stress whereby NO. and ONOO- levels may act as specific inhibitors of this iron-sulphur cluster containing enzyme.
We have studied aconitase activity in platelets from 35 genetically proven HD patients and sex and age matched normal controls.
Here we report a highly significant decrease of aconitase activity independent of medication and sex. We propose that oxidative stress may play a major role in the pathogenesis of HD and is not only reflected in brain but also in other sensitive tissues.

P 3159

Development and validation of the Restless Legs Syndrome Rating Scale-Patient Version (RLSRS-PV)

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Introduction Restless Legs Syndrome (RLS) has been recognized as a neurological disorder since the seminal clinical studies by Ekbom in the mid-20th century. It has a wide range of severity and can be severely disabling. The diagnosis and assessment of severity rely almost entirely on the clinical interview. This study's objective was to validate the RLSRS-PV (adapted from the RLSRS-Investigator Version of the International RLS Study Group) as a possible assessment of RLS severity.
Methods Patients with primary RLS completed the RLSRS-PV twice over a 2-week period. On the second occasion, a trained clinical rater telephoned the patients to ask about changes in symptoms. Analyses were performed to assess reliability, validity and responsiveness.
Results Eighty-five patients completed the questionnaire. The mean (±SD) age when symptoms first appeared was 36.6 (±19.6) years; symptoms began to occur daily approximately 10.5 (±10.3) years later. The average number of missing items per patient in the RLSRS-PV was less than one (0.46 (±1.62)). Factor analysis results suggested that a summary score could be calculated for the questionnaire (Eigenvalue=7.81; cumulative variance=0.56). All items exceeded the test for item-convergent validity (item-scale correlation>=0.4; correlation range: 0.60–0.85). Internal consistency reliability and test-retest reliability also exceeded current criteria (>=0.70). At the 2-week assessment, the scores were sensitive to small clinical changes.
Conclusions The RLSRS-PV is a reliable, valid and responsive patient-reported measure particularly useful for RLS studies as a systematic assessment of RLS severity.

P 3160

Pramipexole in the treatment of restless legs syndrome: a follow up study

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Objective To study the long-term efficacy and safety of pramipexole, a new dopamine D2 -D3 receptor agonist in the treatment of restless legs syndrome.
Methods 16 patients aged 33–75 who participated in a previous open label study were followed for a mean of 6.8 months.
Treatment was started at a dosage of 0.125 mg in every patient administered one our prior to bedtime and progressively increased until the optimal therapeutic effect was obtained. All patients filled out evening and morning questionnaires enquiring about restlessness during the daytime and evening (evening questionnaire) and at bedtime and upon awakenings during the night (morning questionnaire). The questionnaires were filled out one week before, at baseline, one month after treatment and after a mean of 6.8 months of treatment with pramipexole. In these questionnaires, leg restlessness was rated as follows: absence of restlessness =0, mild =1, moderate =2, severe =3.
Results The optimal dosage in this follow up study was 0.125 mg for 8 patients, 0.25 for 3 patients, 0.375 for 2 patients, 0.5 for 2 patients and 0.750 for 1 patient.
The main side effects (nausea for 2 patients, day time sleepiness without sleep attacks for 1 patient and hypotension for 3 patients) were short lasting and of mild severity.
A significant reduction in leg restlessness was found for the bedtime and nighttime measures in all patients with pramipexole administered at bedtime.
Moreover, pramipexole treatment was not associated with morning rebound or afternoon augmentation of leg restlessness.
In addition there was no evidence of a decrease in the therapeutic effect of pramipexole in these patients, even 6.8 months after the initiation of treatment.
Conclusion The study clearly demonstrates that the efficacy of pramipexole does not decrease after 6.8 months of treatment.

P 3161

Hereditary chin trembling: report of a new family, pathogenetic hypothesis and treatment with Botulinum toxin

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Hereditary chin trembling is an unusual dominantly inherited movement disorder characterized by involuntary tremor of the chin with the absence of any other neurological deficits.
Twenty-seven families from Europe, USA, Canada and Latin America suffering from this disorder have been described since 1894.
In this report we present two cases from a new white family, which gives us the opportunity to discuss the origin of the abnormal involuntary movement. The clinical and neurophysiological data lead to the suggestion that hereditary chin trembling is a focal variant of hereditary essential myoclonus localized at the mentalis muscle. We hypothesize that this involuntary disorder may result from hyperexcitability of the lower facial motoneurons.
We have successfully treated them with Botulinum toxin injections to the mentalis muscle.

P 3162

Essential tremor in a Czech patient population – a service based questionnaire study

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Essential tremor (ET) is a chronic condition with a slowly progressive course where upper limbs and, less commonly, head, voice and lower limbs exhibit postural and kinetic tremor without other neurological abnormalities.
To analyse the demographic and clinical correlates of ET in Czech population, a questionnaire was mailed to 320 patients with previously diagnosed ET. The questionnaire included 15 questions and an Archimedes spiral drawing.
We received 164 completed questionnaires (88 females and 76 males, mean age 62 years). The mean age at disease onset was 46.6 years (1–83 years). A positive family history was reported in 46%. Alcohol responsiveness was reported in 33%, however, 43% chose the "don't know" possibility. The most common manifestation was tremor of upper limbs, followed by head, voice and lower limbs. 17% reported the history of treatment with levodopa with a total cumulative dose of 18 to 2700g, the mean duration of levodopa use was 37 months (range 1–120 months).
Spiral drawings were scaled using the modified Bain and Findley Scale (1) that was simplified into 6 grades.
Data obtained in the first questionnaire study concerning ET in Czech Republic do correspond with the results of previously published studies. The high occurrence of inadequate treatment with levodopa shows that ET still may represent a differential diagnostic puzzle. Archimedes spiral drawing appears as a reliable tool for the evaluation of tremor severity and treatment effect.
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P 3163

Spectral analysis of drawing with a digitising tablet for measuring tremor

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Background Digitising tablet is a new computational method for quantification of tremor which results are comparable to the tri-axial accelerometry.
Methods Upper limbs tremor in both hands was assessed in 20 patients with essential tremor and 90 patients with Parkinson's disease. The results of Gibson maze test, rating tremor in spirals and volumetric method were correlated with the results of new technique automatically analysing data from hand-written Archimedean spirals in a virtual triaxial set-up. Tremor intensity was estimated by means of the signal/noise ratio of dominant peak of the power spectrum. The frequency of the highest peak value defined the tremor frequency.
Results Magnitude of tremor based on the speed and acceleration spectrum in the XY axis assessed by digitising tablet correlate with the tremor scores from spiral drawings of both dominant and non-dominant hands, respectively: (Spearman's correlation $R=0.44$, $p=0.00001$; $R=0.46$, $p=0.00001$), Gibson maze test ($R=0.24$, $p=0.03$; $R=0.22$, $p=0.05$) and volumetric methods ($R=0.24$, $p=0.0001$, $R=0.34$, $p=0.003$).

Conclusion A digitising tablet acquisition system is fast, non-invasive, inexpensive and useful as a diagnostic tool. Spiral analysis with digitising tablets could be used as an initial marker of clinical involvement or serve as an objective gauge of change after therapeutic intervention.

P 3164

Clinical assessment of ocular motor disorders in progressive supranuclear palsy, multiple system atrophy and Parkinson's disease

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Objective To determine significant clinical details of ocular motor disorders in progressive supranuclear palsy (PSP) that could help in diagnostic in early and non-typical cases of the disease. To develop clinical scale for assessment of ocular motor disorders in parkinsonism.
Background NINDS-SPSP Clinical Research Criteria for PSP has some weak point which causes misdiagnosis of some cases of multiple system atrophy (MSA) and Parkinson's disease (PD) as PSP.
Design/Methods We have studied 12 patients that met the criteria for possible or probable PSP, 13 patients with possible or probable MSA and 10 patients with idiopathic PD. The Clinical Scale for Ocular Motor Disorders in Parkinsonism (CSOMDP) was developed and prospectively applied.
Results Voluntary saccade slowness was detected in all three groups, though more prominent in PSP patients ($p<0.01$). In 25% of PSP patients jerky character of saccades was lost – "smooth saccades". In 58% there were progressive "wearing off", festination and hypometria of saccades while MSA and PD patients had just bradykinesia and slight hypo-metria of saccades. MSA and PD patients were able to rise saccades speed to normal or at least increase their speed significantly following to the specially given metronome rhythm (according to CSOMDP). In PSP normalisation or significant increase of saccades speed was noted in 33% for horizontal saccades and in 8% for vertical.
Conclusion For PSP diagnostically useful are alteration of character of saccades and patients inability to increase speed of saccades following of the metronome rhythm, as against MSA and PD.

P 3165

MRI imaging of the patients with hepatic form of Wilson's disease

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Objective To detect the sites and frequency of possible lesions applying brain magnetic resonance imaging (MRI) in a group of consecutive, neurologically asymptomatic patients with hepatic form of Wilson's disease (WD).
Patients and methods Sixteen consecutive, neurologically asymptomatic patients with hepatic form of WD (7 untreated and 9 under treatment) were examined with 1.5 T magnetic resonance imager.
Results Abnormal MR brain findings were established in 75% of patients. Lesions in brain parenchyma were detected in all untreated, drug-naive patients and in 44% of treated patients. Abnormal signal in globus pallidus, putamen, and caudate nucleus was revealed in 86%, 71% and 71% of treated and in 33%, 33% and 22% of untreated patients, respectively. In 5 out of 8 patients with putaminal pathology (62.5%) and in 4 out of 7 patients with caudate nuclei involvement (57%), only proton density sequence (PDW) exhibited sensitivity to lesion detection, both with T1W and long echo T2W sequences, having being intensive. This superiority of PDW sequence was even more pronounced in the group of untreated patients whereat 80% of putaminal pathology was visible exclusively on this sequence.
Discussion Majority of our neurologically asymptomatic patients with hepatic form of WD had MRI findings, suggesting to different brain lesions. Lower frequency of such lesions in the group of treated patients in comparison to untreated ones, indicated that they might be reversible (chronic chelating therapy). Finally, our results suggest that PDW sequence still plays an important role in correct MR detection of brain lesions in these patients.

P 3166

Spreading of primary dystonia

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P 3167

Electromyographic findings in myasthenia gravis concurrent pathologies

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P 3168

A contribution to the problem pf balance preservation in spinal cord injured patients

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Cognitive neurology

P 3169

The short aphasia-check-list: an economical screening for detecting aphasia

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Introduction In clinical practice an economical diagnosis of aphasia is important for identifying patients who are in need of speech therapy and/or pharmacotherapy. However, most aphasia tests require too much time for General Practitioners. We developed the "Short-Aphasia-Check-List" (German: Kurze-Aphasie-Check-Liste, ACL-K), which is a short but sensitive test for detecting aphasia in brain-damaged patients.
Methods In the normation, study 148 aphasic patients (AP, mean age=62.7yrs. SD=15.2) and 104 controls (CG, mean age=57.9yrs. SD=17.2) were included. All subjects were tested with the longer German test-battery "Aphasia-Check-List" (ACL, Kalbe et al., 2002), and the AP with the Aachen-Aphasia-Test (AAT). For the ACL-K those subtests of the ACL were selected that suited best for a quick but sensitive diagnosis of aphasia.
Results A combination of four subtests was chosen: a colour-figure-test (modification of Token Test), a verbal fluency task (supermarket), a reading task and a rating for verbal communication. The test administration takes approx. 10 minutes. Due to a significant age, effect ($p<.001$) age-corrected scoring was defined for the supermarket task. After subtests were weighted, (considering statistics and contents) the maximal transformed score of the ACL-K is 40 points. With a cut-off of 33 points (<33=impaired), sensitivity of the ACL-K is 94.7%, specificity 98.1%. On the basis of the AP scores, the "pathological range" under 33 was subdivided into intervals for mild (26–32), moderate (15–25), and severe (0–14 points) language impairment that corresponded well to the impairment severity in the AAT.
Conclusion The Short-Aphasia-Check-List (ACL-K) is an economical, valid and very sensitive instrument to detect aphasia and describe its severity.

P 3170

Cerebral blood flow SPECT imaging in right hemisphere-damaged patients with hemispatial neglect

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Background Hemispatial neglect is characterised as a failure by the patient with stroke to attend to contralesional space. It is hypothesised to be a result of damage to a network involving the frontal, parietal, and cingulated cortices, basal ganglia, and thalamus.
Methods The aim of this preliminary study was to verify this model of neglect in 22 right hemisphere-damaged acute stroke patients using single photon emission-computed tomography (SPECT). Presence of a single right-sided vascular brain lesion was confirmed on CT and/or MRI. Hemispatial neglect, assessed with a battery of drawings, line bisection, and line and shape cancellation tests, was observed in 12 cases.
Results Patients with neglect (compared with those without neglect) had more extensive hypoperfusion in the frontal and parietal cortex, as well as striatum and thalamus. Left-sided hypoperfusion in the parietal cortex and the thalamus was also significantly associated with neglect on SPECT imaging. Performance on three out of five tasks of psychological assessment commonly used to detect the presence of hemispatial neglect was exclusively linked with damage of the parietal cortex of the right hemisphere, while the line cancellation test might be attributable to the lesion of the right striatum.
Conclusions This findings support the model attributing hemispatial neglect to a unilateral defect in a cortico-striato-thalamo-cortical loop. CBF SPECT imaging may provide a reliable description of the brain pathology associated with hemispatial neglect.

P 3171

Cognitive deficits in depressed and non-depressed Parkinson's disease patients

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Introduction Neuropsychological deficits, as well as, depression are the most frequent and important non-motor findings in patients with Parkinson's disease (PD). The major aim of the study was to determine if there was a specific association between depression and cognitive impairment in PD.
Methods A consecutive series of 102 patients with idiopathic PD: major depressed (n=31, mean age=55.6±2.1), minor depressed (n=29, mean age=58.3±1.8) and non- depressed PD patients (n=42.58, 1±2.9) matched by age, sex, education, and severity of PD were included in the neuropsychological investigation. The Wechsler Adult Intelligence Scale-Revised form (WAIS-R) was applied as a measure of the global cognitive functioning. Also, the frontal sensitive tasks were included in the protocol: fluency tests, Trail Making Test (TMT) and the computerized Cambridge Neuropsychological Test Automated Battery (CANTAB).
Results The depressed PD patients were inferior on WAIS-R subtests: Picture Completion Task ($p=0.001$), Block design ($p=0.01$), and Symbol Digit Modalities ($p=0.007$). The significant differences between minor depressed and non-depressed PD patients were obtained on fluency tasks ($p=0.004$), attentional set shifting task ($p=0.011$) and spatial working memory test ($p=0.041$). Also, it was shown that the depressed PD patients were inferior to the non-depressed PD subjects on problem-solving tasks ($p=0.020$).
Conclusions The present study showed the specific cognitive pattern of impairment in depressed PD patients in frontostriatal sensitive tasks, with additional deficits recorded in visuo-spatial memory domain. The findings differed in comparison to frontostriatal profile of deficits usually seen in PD patients.

P 3172

Quantitative EEG changes during cognition tasks in patients with cognitive impairment.

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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.
Cognition tasks during ongoing qEEG-registration reveal significant abnormalities even in cases of subtle cognitive impairment.

P 3173

Depression in epilepsy and migraine: a comparative study in children

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Objective This study was designed to compare the severity of depression occurring in children with migraine and epilepsy.
Backgrounds Comorbidity of depression with the general medical conditions is common. Studies have identified high rates of mood disorder in children with various neurological disorders, including migraine and epilepsy. Migraine and epilepsy might share a common pathophysiology. Children with migraine have 3% to 7% incidence of epilepsy. Comorbidity of depression with epilepsy and migraine may provide clues to pathophysiology and any shared mechanisms of the two disorders.
Design and methods We administered Arabic Children's Depression Inventory (ACDI) and Child Depression Inventory (CDI) to 20 children with migraine, 20 children with primary generalized tonic clonic seizures (GTCSs) and 20 age- and sex-matched healthy control children. The age range of all children was 7–15 years. Demographic, socio-economic, and number of attacks were examined in relation to depression scores.
Results Depression scores on both the CDI and ACDI were significantly higher in the epilepsy and migraine groups than in the control group. There was no statistically significant difference between the mean scores of the CDI and ACDI in the epileptic (53.9 ± 15.2 & $54.2+16.7$) and migraine children (47.7 ± 9.8 & 48.4 ± 11.6) $p>0.05$.
Conclusion Epileptic and migraine children have equally high depression severity.

P 3174

Déjà vu, jamais vu? Capgras syndrome between perception and memory

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Capgras delusion, the belief that an identical impostor has replaced a close relative, has been increasingly reported in brain-damaged patients. The syndrome challenges models of face-person recognition system because of its paradox of identifying a person and at the same time denying its authenticity. This clinical condition has recently become the focus of lively speculations (Ellis and Lewis, 2001).
Fred (a fictitious name) presented with progressive dementia hallmarked since onset by persistent Capgras delusion concerning his wife. Time passing Fred produced multiple reduplications of her. The disease progressed to several delusional misidentifications (including mirror misidentification of himself) and eventually gave way to a full-blown frontal syndrome. Formal assessment of face processing ability disclosed selective impairment in familiarity judgment, with a strong tendency to falsely recognize unfamiliar people.
We surmise that richness and fluidity of Person Identity Nodes (PINs) related to highly familiar people, characterized by multiple exposures and multi-modal experiences, lead to intrinsic fragility of matching of continuously changing, multifaceted perceptual information with already stored representations ("exemplar semantics"– Gentileschi et al., 2001). Linking of successive temporal perceptual experiences to a unitary person representation may be impaired by frontal damage, thereby producing reduplication.
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P 3175

Qualitative differences of "Theory of Mind" (ToM) impairments in Schizophrenia

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Introduction "Theory of Mind" (ToM) refers to the ability to see the world from another person's point of view and hence be able to understand their mental states. Evidence suggests that schizophrenics have a deficit in ToM. Here, we are trying to further investigate the nature of this deficit.
A quantitative and qualitative data analysis is performed to elucidate whether ToM-deficits observed in schizophrenics are either due to problems in attributing mental states (emotions, thoughts, intentions) to others per se, or to a misinterpretation of perceived inner worlds of others.
Methods To date, 16 schizophrenics (mean age 28.8 years; SD 9.6) have been compared with 10 age and education-matched controls on their performances in modified and self-developed ToM tests and neuropsychological measures.
Results Schizophrenics were slightly impaired in some cognitive tasks whereas they exhibited highly significant deficits in ToM tasks. Their difficulties were most prominent ($p<0.001$) in a task requiring the subject to attribute thoughts to others (patients: median=12.0; range 6–15; controls: median=15.5; range 12–16; max=16) as well as in a task involving recognition of emotions (patients: mean=21.9; SD=2.2; controls: mean=25.7; SD=1.1; max=28). In another ToM task, patients tried to imagine themselves in another person's shoes (patients: median=16.0; range 8–16; controls: median=16.0; range 15–16; max=16), but scored lower ($p<0.001$) (patients: mean=9.1; SD 3.9; controls: mean=14.6; SD 1.3; max=16) because of misinterpretations of the characters' actual mental state.

Conclusion Slightly cognitively impaired schizophrenics exhibit clear impairments in ToM measures. This deficit however is not due to a general inability of attributing mental states to others but rather to a tendency to misinterpret them.

P 3176

Decision-making in obesity: A study with gambling task

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The Gambling Task (GT) is a test that was devised to detect impairments in personal and social decision-making. Evidences of failure in making long-term advantage choices were found in patients with pre-frontal cortex damages, obsessive-compulsive syndromes and in substance abusers. Aim of the study was to investigate if also severely obese people could show an "impulsive" behaviour that doesn't take care of long-term disadvantages.
We utilized a PC-implemented version of GT: Participants were all presented with four decks of cards (labelled A, B, C and D) and a loan of 2000 $. They were told to try to maximize the profit on the 2000 $ by choosing one card at a time from any of the four decks. Additionally, they were informed that some of the decks were worse than others and to try to avoid them. They didn't know when the task would be stopped (after 100 choices).
We tested a group of 10 patients affected by severe obesity (BMI >34), who were not identified as "pathological" to usual psychological test evaluating personality and food behaviours. The group of control consisted of 27 young adult people with a normal weight.
Our results show a different pattern of performance between the groups: Controls make a constant increase of advantageous choices during the task, while obese didn't, rather showing random shifting between the two kinds of decks.
These preliminary data seem to give evidence of impulsivity in decisional behaviours of obese people, which are not revealed by traditional psychometrical tests.

P 3177

Therapy of attentional deficits by telerehabilitation: improvements and their stability

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The Fachklinik Herzogenaurach in cooperation with Dr. Hein GmbH developed a software package for telerehabilitation, which allows composing an individual neuropsychological training program. The patient can perform this training program in the clinic or at home. The therapist supervises and adapts the training on the basis of a continuous feedback on the performance of the patient.
To check the practicability and the effects of this system we performed a control group study in a matched pair crossover design with outpatients suffering from acquired brain lesions with persisting attentional deficits. N=62 subjects had been assigned to two groups (A and B). Group A got 11 weeks of training while group B has been waiting. Then the treatment plan changed. During the training, the participants met the therapist in the clinic once a week. Neuropsychological and medical examinations took place before, between and after the two training periods.
Because of dropouts N=40 subjects remained in the study. The effectiveness of the training is sustained by the fact that in the first part of the study considerably more subjects in the training group reached their neuropsychological therapy goals than did members of the control group. 64% of these subjects could keep their improvements. 56% of the subjects in the training group who did not reach their therapy goal during the training period could reach this goal afterwards. No negative, but positive medical and psychosocial side effects could be proven.

P 3178

Effect of Cavinton on cognitive functions in Parkinson's disease

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Neuroprotective effect is the most significant among the therapeutic actions of vinpocetine. It is related to the inhibition of operation of voltage dependent neuronal Na (+)-channels, indirect inhibition of some molecular cascades initiated by the rise of intracellular Ca (2+)-levels and inhibition of adenosine reuptake.
The **aim** of the study was to test the effect of Cavinton (vinpocetine) on cognitive impairment in Parkinson's disease (PD). A 3-month open trial with Cavinton was carried out in 15 patients (58–72 yrs) with PD (Hoehn & Yahr stage I) and mild cognitive deficit (MMS>20). Cavinton was given orally in tablets (10 mg) 3 times daily. All other treatment remained unchanged. The patients were examined before and after treatment course by a battery of neuropsychological tests (Digit Span Forward; 10 Words Learning Test; Digit Span Backward; Trail Making Test; Stoop Test; Similarities; Verbal Fluency) and Sung Depressive Scale. After Cavinton treatment the MMS total score was increased with 1.5 points ($p>0.05$). A significant ($p<0.05$) improvement in test for long-term memory and some tests for executive functions (Stoop Test, Verbal Fluency) was found. The mood state was not changed. There were no significant side effects in patients.
Conclusion was drawn that Cavinton is suitable for treatment of patients with PD presenting cognitive deficit. The favourable effect of Cavinton on the cognitive functions could be connected with its complex effect.

P 3179

Changes in complex attention in multiple sclerosis patients receiving interferon-beta-1b

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Patients with multiple sclerosis (MS) have consistently been found to display attention deficits on more complex tasks requiring mental tracking or visuomotor tracking. Significant improvement of complex attention, concentration as well as visual learning and recall was recently reported after 1 year of treatment with interferon-beta-1 b (INF beta-1b) (Barak & Achiron, 2002).
The objective of present study was to explore the effect of INF-beta-1b on different attention characteristics from simple auditory span to aspects of attention closely related to working memory and executive functions.

Subjects were 24 women with relapsing-remitting MS, mean age 35 years (20–53). They were tested at the beginning of the treatment and at 14th–16th week of INF-beta-1b application, 10 of them underwent third assessment at 32nd–36th week. The neuropsychological battery included Digit Span, Digit Symbol, Trail Making Test (A, B), Paced Auditory Serial Addition Test (PASAT) and Stroop Test.
The results demonstrated significant improvement of concentration (Digit Symbol), complex attention and speed of information processing (PASAT) as measured by number of correct responses and number of omissions at rate 3 sec of stimulus presentation.
It appeared that reduced speed of information processing and working memory capacity was improved after INF-beta-1b treatment.

P 3180

Depression in patients with Parkinson's disease

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Introduction Depression is common and may occur at any stage in the history of Parkinson's disease. Its rate in patients with Parkinson's disease vary because of differences in definition of depression, difficulties in distinguishing between features of depression and those of Parkinson's disease, methods of assessment, and patient population studied.
Objectives To measure the rate and severity of depression among patients with Parkinson's disease (PD), and its correlation with motor disability, age, sex, and other variables.
Methodology 54 patients with PD were matched for age and sex with 52 healthy controls, depression was diagnosed by using ICD-10 criteria and its severity was rated by Beck Depression Inventory while the motor disability of PD was made according to Hoehn and Yahr scale.
Result Patients group was significantly more depressed than the control group (42.59% Vs 7.69%, $P<0.001$) and there is a probable correlation between the severity of depression and severity of motor disability ($P<0.05$).
47% of depressed patients were in the age group (50–59) years, and the rate of depression was nearly equal between sexes.
Conclusions Parkinsonian patients suffer a degree of depression that cannot only be attributed to the reaction to motor disability, but there is an underlying neurochemical disturbance.
Reference
Cummings JL (1992). Depression and Parkinson's disease, a review American Journal of Psychiatry. 149: 443–454.

P 3181

Neuropsychological and neurological correlates preverbal forms of speech communication (baby-prattle and childish babble) in diagnostics of morpho-functional clinico-neural disorders with young children

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Modern development of neuropsychological diagnostics of higher psychic function disorders both with adults and children (at different cerebral pathology– from slight cerebral dysfunction to its acute manifestations at morpho-functional lesions) is characterized by quite high resolvability of neuropsychological qualitative factorial analysis and quantitative evaluative methods. Application of the latter in the infant neurological practice prevails with the early-aged children.
Neuropsychological analysis and psycholinguistic evaluation of pre-verbal communication (baby-prattle and childish babble) with early-aged children (6–12 months) in the diagnostics of morpho-functional disorders of nervous system functioning may gain special significance, as in this very period innate reflexes (on which bases diagnostics of child's nervous system disorders is being carried out) become too extinct and conditioned reflexes manage not to develop entirely. Neurological "diagnostic vacuum" (author's definition) arises, determining the faults of diagnostics of different central nervous system (CNS) parts functional and organic disorders. Pre-verbal communication (particularly childish prattle), which may play important diagnostic role in evaluation of functional state of cerebral structures and blocks of brain, begins to rapidly develop within this very period of child's development.
During our research the goals of the development of neuropsychological, clinico-neural, psycholinguistic correlates and preverbal communication forms (baby-prattle and childish babble) complex evaluation, as well as the study of neuropsychological mechanisms of cerebral dysfunction in the acts of baby-prattle and childish babble in accordance with data of additional methods of verification of morpho-functional disorders (MR-imaging, Doppler ultrasound, electroencephalogram (EEG), Echoencephalogram, and etc.) were accomplished within the framework of neurological-neuropsychological diagnostic and rehabilitation centre.

P 3182

Computer simulation of alternative splicing underlying the strength of a glutamatergic synapse

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Introduction A hypothetical model of the mechanisms involved in the process of memory formation and forgetting at the level of a glutamate synapse is presented. The process of memorizing and forgetting is described by means of two independent variables: retrievability and stability.
Methods Alternative splicing is proposed as the basis of the regulation of the synaptic strength. In the model, the population of N-methyl-D-aspartate (NMDA) receptors changes its proprieties during the learning process. Object Pascal is used to implement a mathematical model of the synapse and to simulate the changes of the properties of the synapse in time in the learning process.
Results The computer model developed along the concept of the two independent variables of memory makes it possible to simulate synaptic properties such as conductivity, sensitivity, spacing effect, desensitisation, forgetting, phosphorylation, the number of the NMDA and AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic) receptors, and other parameters.
Conclusion The computer implementation makes it possible to easily analyse and verify the model at both conceptual and mathematical level, and provide guidance to experimental research, determining what sort of new data might serve falsification or corroboration of the model. This is a new, original explanation of the mechanisms involved in the memory formation at the molecular level. This model can explain both short-term and long-term memory formation. The changes in the population of NMDA receptors in the postsynaptic membrane are necessary for the memory formation.

P 3183

Clinicopsychological syndromatics and circadian profile of arterial blood pressure (ABP) under angioencephalopathy

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Neuroimaging

P 3184

Can intramedullary signal hyperintensity on magnetic resonance imaging predict the outcome of surgical treatment in cervical spondylotic myelopathy?

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Introduction There is no evidence as to whether the presence of magnetic resonance high signal intensity areas in the spinal cord can be a predictor for surgical results in patients with spondylotic cervical myelopathy.
Material and methods This is a prospective 3-year follow-up study comprising of 42 patients with cervical spondylotic myelopathy who underwent surgery. The clinical outcome was measured by means of the mJOA score, a timed 10-m walk and the patients' subjective evaluation of satisfaction with the surgery. Twenty-two patients showed high intensity areas in the spinal cord on the T2-weight image and twenty patients had normal intensity.
Results On average, no significant differences in mJOA score and in the timed 10-m walk test were observed over the 36 months of follow-up in comparison with the pre-treatment period. Subjective score improved in 58% of patients, remained identical in 20%, and deteriorated in 22% at the 6-month time point. However, at the 36th month the subjective state was declared as improved in 15%, identical in 41%, and deteriorated in 44% of patients. There were no differences between the group with the high intensity areas and those with normal findings on magnetic resonance imaging.
Conclusions The current study did not demonstrate significant changes in objective parameters over 36 months of follow-up in surgically treated patients with SCM. A significant number of patients deteriorated in subjective assessment. The presence or absence of high signal intensity areas in the spinal cord had no power to predict the outcome of the surgical treatment.

P 3185

Magnetization transfer analysis of multiple system atrophy

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Objective To determine whether magnetization transfer imaging (MTI) demonstrates characteristic abnormalities in the brain structures of patients with multiple system atrophy (MSA).
Patients and methods Twelve patients with clinically probable MSA and 11 control subjects were examined. From MTI, magnetization transfer ratios (MTRs) were calculated using region of interest analysis. Abnormal signal changes in the base of the pons, middle cerebellar peduncle, and putamen were assessed on T2-weighted images.
Results MTRs of the base of the pons, middle cerebellar peduncle, putamen, and white matter of the precentral gyrus were significantly lower in the MSA patients than in the controls. Abnormal signal changes on T2-weighted images were observed as follows: hyperintense signal changes in the base of the pons in 6 patients and in bilateral middle cerebellar peduncles in 7 patients, a combination of hyperintense and hypointense signal changes in the dorsolateral portions of bilateral putamen in 3 patients and of the unilateral putamen in 2 patients, and hypointense signal changes alone in the dorsolateral portions of bilateral putamen in 2 patients. MTRs of regions with abnormal signal changes were significantly lower than those of regions without abnormal signals and than those in the controls. Even the MTRs of the regions without abnormal signal changes were lower than those in the controls.
Conclusions MTI demonstrates characteristic abnormalities in the brain of patients with MSA that seem to reflect underlying pathological changes, and the abnormalities are detected more sensitively and over a larger area by MTI than by conventional magnetic resonance imaging.

P 3186

fMRI detects activation in the sensorimotor cortex before and after subsensory whole-hand afferent electrical stimulation in humans

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Introduction The aim of the study was to elaborate, whether changes in the motor cortex activation pattern can be demonstrated after electrical stimulation of the hand in volunteers.
Materials and methods All experiments were performed on a 1.5 Tesla MR-scanner. The motor-paradigm was self-paced finger-to-thumb-tapping of the left hand.
The experimental set-up consisted of a baseline fMRI examination using the above-mentioned motor-paradigm. Then, sub threshold electrical stimulation was applied for a duration of 20 minutes to the left hand using a mesh-glove, outside the magnet. This was followed by another fMRI run identical to the baseline examination. The entire experiment was performed twice at different days.
Post processing was done with SPM99.
Results The base-line fMRI examinations revealed activation of the primary and secondary motor cortex as previously described. After electric stimulation of the left hand, there was a quantitative increase of activated pixels in these areas. In addition, there was activation of regions not visible on the base-line studies. These involved the ipsilateral lobus parietalis inferior and the contra lateral gyrus precentralis, gyrus postcentralis and lobus parietalis superior. This pattern was observed in all volunteers and also when the experiments were repeated on another day.
Conclusions We have demonstrated, that afferent electrical whole-hand stimulation with a mesh-glove in fact leads to a lasting change in the responsiveness of the human brain to a motor paradigm. Nevertheless, the results of this initial study

could show in vivo that motor activation patterns can be successfully influenced by sensoric stimulation of afferent pathways.

P 3187

fMRI detects functional plasticity of the sensorimotor cortex after upper extremity amputation

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Purpose In this study, we looked for functional plasticity in the SM1 in a patient who sustained a right upper extremity amputation.
Methods The perioral region bilaterally, the stump on the right side on the location where the former (phantom) middle finger (PMF) was sensated and the existent middle finger (EMF) on the left side was stimulated with 2 Hz. Finally the patient imagined fist clenching of the amputated and the normal hand.
All experiments were performed on a 1.5 Tesla MRI-Scanner. Post processing was done with SPM99.
Results Sensorimotor brain areas could be differentiated within both hemispheres.
Imagination of fist clenching led to a spatial difference of the activation foci in the primary motor cortex (M1) within the two hemispheres in the range of 4-12 mm.
The tactile task within the labial angle of the right perioral region lead to a cranial shift of the cortical representation of the perioral region within the contra lateral somatosensory cortex (S1) invading the former cortical representation of the amputated limb up to 15 mm.
The tactile task of the PMF within the stump showed a cranial shift on the convexity up to 8 mm in contrast to the SM1 activation focus of the EMF.
Conclusion In concordance with previous studies, we observed a clear reorganization phenomenon within SM1 of a patient with phantom limb pain after upper extremity amputation 29 years ago. The result of the current study can be interpreted as evidence for plasticity within the sensory cortex following traumatic limb amputation.

P 3188

Functional magnetic resonance imaging of the sensorimotor cortex of the lower limbs by means of a force controllable actuator

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Purpose The aim of the study was the implementation of a vibrotactile stimulation paradigm within the MR environment in healthy volunteers for further clinical application in patients with severe motor deficits.
Methods 10 healthy, male volunteers performed a foot-tapping paradigm with the right foot. In a second experimental run, the subject's sole was vibrated with a force controllable electromagnetic actuator. The vibration stimulus within a frequency range from 0–100 Hz in steps of 10 Hz was applied onto the sole of the right foot above the basic joints of the toes I–V.
All experiments were performed on a 1.5 Tesla MR-Scanner with T2*-weighted single shot echo-planar sequences. Post-processing was done with software SPM99.
Results Group analysis showed:
1. For the foot tapping paradigm (FTP) cortical brain activation within the contralateral hemisphere within the Gyrus precentralis (GPrC, MI), Gyrus postcentralis (GPoC, SI), Lobulus parietalis inferior (LPi, SII) and Gyrus cinguli (GC). Ipsilateral brain activation could be detected within the LPi, GPoC and LPs.
2. For the vibrotactile stimulation of the sole of the right foot (VPD) brain activation could be elicited contralaterally within the GPrC, GPoC, LPi, GC and Gyrus frontalis superior (GFs) and ipsilaterally within the LPi and the LPs.
Conclusion In our study, we implement an MR compatible moving coil actuator, which can easily be controlled and which can be applied for detailed functional maps of the sensorimotor cortex for the lower extremities especially for patients with spinal cord injury and damage of the long tracts.

P 3189

Thrombosis of dural sinuses: comparison of magnetic resonance imaging (MRI) and MR-angiography (MRA) with multislice (MS)-CT and CT-angiography (CTA)

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Purpose Comparison of unenhanced MS-CT combined with CTA and the "gold standard" MRI combined with MRA in the diagnosis of dural sinus thrombosis.
Material and methods In a prospective study 71 patients with the clinical suspicion of thrombosis of dural sinuses were examined with unenhanced cerebral MS-CT combined with CTA (coll. 1mm, pitch 3, 100 ml CM, flow velocity 4 ml/sec) and with cerebral MRI (TSE T2 axial, FLAIR axial, FFE coronal, TSE T1 sagittal) combined with MRA (TOF axial, PCA sagittal/axial with flow-velocity 30 sec, with MIP-reconstruction). Three-experienced radiologist evaluated all examinations for thrombosis in cerebral sinuses and graded the detectability of the concerned cerebral veins. All patients were followed either clinically or with CT or MRI to verify the diagnosis. Interobserver agreement was calculated with kappa-statistics. Examination time of CT and MRI was compared.
Results MS-CT and CTA revealed sinus venous thrombosis in 22 patients, MRI and MRA in 20 patients. Thromboses were detected with CT in 43 dural sinuses and 13 cerebral veins and with MRI in 38 sinuses and 6 cerebral veins. One patient showed dural venous fistulas with multiple venous collaterals as complication after thrombosis of dural sinuses in CTA and MRA in equal quality. CT and MRI showed in 48 patients no dural sinus thrombosis. In 2 patients, MRI could not differentiate between hypoplasia and thrombosis of transverse sinus. The interobserver agreement was 100% with CT and 94% with MRI. The average time that the examinations lasted were 10 minutes in CT and 35 minutes in MRI.

Conclusion Thrombosis is detected with CT more accurately and with higher interobserver-agreement than with MRI. Examination time is significantly shorter with CT than with MRI.

P 3190

Blood flow and acetazolamide vasoreactivity in post-hypoxic-ischaemic amnesia: a positron emission tomographic study

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Introduction Despite extensive research it still remains controversial as to what the precise location of the critical lesions underlying amnesia actually is. The amnestic syndrome is believed to be heterogenous and due to several distinct functional deficits.
Patients and methods Two patients, a 45 year-old woman and a 56 year-old man, respectively with sudden cardio-pulmonary arrest and successful reanimation, were left with a clear amnestic syndrome as main neurological sequela. During their revalidation period, they underwent a positron emission tomographic (PET) examination, utilizing the ^{13}NH3 bolus technique at rest and after intravenous acetazolamide administration.
Results Both PET studies showed more or less similar features with global decrease of regional cerebral blood flow (rCBF) in frontal, temporal and parietal lobes. In addition, rCBF was increased in both thalami of the 45 year-old patient and in the basal ganglia of the 56 year-old man. Acetazolamide vasoreactivity was most lost in the frontal lobes.
Conclusions In the present PET study we demonstrated that destruction of the inhibitory pathways to thalamus and basal ganglia by hypoxic-ischaemic frontal lesions could be one of the mechanisms leading to amnesia.

P 3191

Diffusion weighted MR findings in isolated angiitis of CNS (IACNS)

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Introduction The diagnosis of isolated angiitis of CNS (IACNS) has been problematic, mainly a process of exclusion, and requires biopsy for confirmation. However, brain biopsy has limited sensitivity due to the dependency on the site of the biopsy. The new non-invasive diagnostic test is required. Diffusion weighted imaging (DWI) findings in vasculitis are rarely reported. We report DWI findings of two cases with IACNS.
Methods A 31-year old woman and a 40-year-old woman with recurrent stroke-like episodes and seizures are reported. The diagnoses of these patients were made by the multiple lesions in the conventional brain MR and the typical cerebral angiographic findings with prominent changes over a short period, negative results of the extensive search for the risk factors of atherosclerosis, embolism, systemic vasculitis and other systemic diseases. The DWIs with ADC maps were performed within 3 days after the symptom onset.
Results DWIs obtained 2 or 3 days after the symptom onset showed bright hyper-intense lesions with some slightly hyper-intense lesions. ADC values in the bright hyper-intense lesions were 399 to 551 ¥10^{-6} mm^2/s that indicate cytotoxic oedema and slightly hyper-intense lesions were 948 to 1196 ¥10^{-6} mm^2/s that indicate vasogenic oedema.
Conclusion DWI with ADC map in IACNS shows heterogeneous signal intensities that suggest the various stages of inflammatory process with ischemia and allow differentiation from usual arterial infarction. DWI with ADC map can be a useful non-invasive diagnostic test increasing specificity in the diagnosis of IACNS, combined with conventional MRI and cerebral angiography.

P 3192

A rare cause of stroke: left atrial myxoma. A report of two cases

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Introduction Myxoma is the most common primary cardiac tumour. In 50% of the cases, the first manifestation of the tumour is cerebral embolisation due to thrombus formation on its villous surface. A rare complication of myxoma can be cerebral metastases and formation of aneurysm.
Materials and methods We present two middle-aged patients; a female with ictal mild right-sided hemiparesis, and a male with ictal vertigo, nystagmus, internuclear ophthalmoplegia (INO) and gait disturbances. Neither of them had any symptoms referring to a cardiac disease.
Results CT and MR showed multiple cerebral infarcts, besides there were T2 hyperintense foci in periventricular white matter and in the thalami. Transthoracic and transoesophageal echocardiography revealed the left atrial myxoma, which was treated by surgical excision.
Conclusion In case of multiple cerebral infarcts, we should think of myxoma as well as a possible cause, even if there is not cardiac symptoms or history. Early diagnosis and surgical treatment can prevent further embolisation. When myxoma is justified a careful search for cerebral metastases and aneurysm is necessary.

P 3193

Transcranial Doppler evaluation of arterial occlusive disease in aphasic patients

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Background and purpose Aphasia is a sign of cortical involvement in stroke patients, affecting the dominant hemisphere supplied by the middle cerebral artery (MCA). The diagnose of MCA occlusion is connected with transport to radiology. In order to evaluate the localization of arterial occlusive disease, we evaluated acute aphasic stroke patients by means of transcranial Doppler (TCD).
Patients and methods We investigated 30 ischemic stroke patients admitted within 24 hours from stroke onset. All patients were right handed, except one, and fulfilled the criteria for aphasia according to the Boston Diagnostic Examination of Aphasia. TCD was performed bedside with DWL Multi Dop XL, 2 MHz transducer. Thrombolysis in brain ischemia (TIBI) criteria was applied for localization of the MCA occlusion.
Results Out of 30 patients, 6 had left M1 MCA occlusion, one right M1 MCA occlusion, 4 left M1 MCA stenosis, and 6 left M2 or M3 occlusion, and 9 hypo-perfusion. Early ischemic signs in left MCA territory were visible in 27 patients. 9 patients had left internal carotid artery (ICA) subtotal stenosis

(3 intracranial, 6 extracranial), and 7 left ICA occlusion (1 intracranial, 6 extracranial) and one right ICA occlusion.
Conclusion TCD is a useful and non-invasive method for bedside evaluation of MCA occlusive disease in acute stroke patients with aphasia.

P 3194

Three-dimensional ultrasound of the Willis circle and the vertebrobasilar system

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Background and purpose Transcranial colour-coded sonography (TCCS) is used for evaluation of the Willis circle and vertebrobasilar system (VBS). Freehanded noncontrast three-dimensional ultrasound (3D US) enables reconstructions from transcranial power Doppler (PD) imaging of the Willis circle and VBS.
Patients and methods We displayed the 3D images of the Willis circle and VBS. Data acquisition was performed using 2.5 MHz sector transducer (Aloka Prosound SSD-5500), freehanded during 10 seconds, allowing PD sonography and post processed (Tom Tec imaging systems). The technique was applied in 10 patients.
Results One patient was excluded due to inadequate bone window. TCCS enabled visualization of only colour coded flow of all circle of Willis vessels simultaneously in one patient and all vessels of the VBS was not possible at all. Post processing and skilled rotation 3D PD data sets enabled visualization of the one side of the Willis circle in all patients but two, where only part of one arterial segment couldn't be displayed. Visualization of the communicating arteries or collateral flow in patients with occlusive disease was good. Hemodynamic analysis in TCCS was indispensable for occlusive disease evaluation and collateral pathways interpretation. 3D PD enabled visualization of all three vessels of the VBS simultaneously, allowing interpretation of the BA origin (neither patient had occlusive disease of that segment).
Conclusions Noncontrast 3D US enables display of one side of the Willis circle or VBS simultaneously in most patients. TCCS and hemodynamic analysis is needed for the evaluation of the occlusive disease and interpretation of the collateral pathways.

P 3195

Effect of laser acupuncture of the visual association cortex in humans: a functional magnetic resonance imaging study

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Purpose The use and efficacy of acupuncture treatment are not yet widely accepted in western medicine. Demonstration of specific acupuncture effects on relevant structures of the human brain would facilitate acceptance of this therapeutic modality into the practice of modern medicine. The aim of this study was to investigate the effect of laser acupuncture on the cerebral cortex.
Methods With functional Magnetic resonance imaging (fMRI) cortical activations during laser acupuncture and dummy acupuncture were compared using a block design in 10 healthy male volunteers. Therefore, we used the acupoint BL 67 (VA1), which is located on the lateral aspect of the foot and acupuncture was applied to the left foot. All experiments were done on a 1.5 Tesla MR-scanner equipped with a circular polarised head coil. Post processing was done with SPM99.
Results During laser acupuncture we found activation in the cuneus corresponding to Brodman Area (BA) 18 and the medial occipital gyrus (BA 19) of the left visual cortex. Placebo stimulation did not show any activation.
Conclusion We could demonstrate, that laser acupuncture of a specific acupoint, empirically related to ophthalmic disorders, leads to activation of visual brain areas, whereas placebo acupuncture did not. Furthermore, we got similar activation pattern like a further needle acupuncture study by Cho et al. at the same acupoint. These results indicate, that laser acupuncture has a similar effect on the cerebral cortex like needle acupuncture and thus can give further evidence for the effectiveness and therapeutic potential of laser acupuncture.

P 3196

SPECT studies in vascular dementia

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Vascular dementia is a very difficult disease for diagnosis. Owing to the new methods in last time, the diagnosis of vascular dementia is easier.
The study was performed in 37 patients in age 48–85, mean 67. SPECT and CT were carried out in all patients. In CT, it was observed two and more ischemic lesions in brain. To the group with dementia patients were classified according to criteria of DSM-IV, ICD-10, MMS and Hachinsky Ischemia Scale. Apparatus APEX SP 6 HR firm Elscint using complex of 99m-Tc-ECD performed SPECT.
Results It was observed many hypo dense lesions in all patients with dementia, especially in temporal and frontal lobes. These results were compared with CT results. It was found conformability of lesions localisation in both examinations. However, the hypo dense lesions in SPECT were bigger than lesions in CT. It was observed many ischemic lesions in SPECT, invisible in CT.
Conclusions SPECT is more sensitive examination than CT in diagnosis of vascular dementia. SPECT should be the primary examinations in diagnosis of vascular dementia in the results of CT are negative.

P 3197

Usefulness of SPECT study in TIA

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The **aim** of the study was to evaluate the brain perfusion differences using Single Photon Emission Computed Tomography (SPECT) in patients with transient brain ischemia. Patients with transient ischemic attacks originating from the internal carotid artery and the basilar artery were qualified for the study.

Neurological focal symptoms retreated at all patients up to 24 hours. Obtained results were compared with a control group.
The study was based on data gained in total of 50 patients (24 male, 26 female, mean age 50 years, range 37–70). The brain perfusion was assessed by SPECT examination with gamma-camera device (Elscint type Apex SP-6 HR). All patients underwent Computed Tomography (CT) and Transcranial Doppler (TCD) sonography, where no significant pathology was found. Obtained results allowed to divide patients into three groups:
I – perfusion disturbances were found in temporal lobe (14 patients),
II – perfusion disturbances in occipital lobe (11 patients),
III – no pathology was found.
Results SPECT diagnosis is one of the most sensitive methods of the brain perfusion evaluation. The brain perfusion evaluation allows finding vascular originated pathology. Multidimensional microcirculation visualization of the existing symptoms correlates with patient's clinical status.

Multiple sclerosis 2

P 3198

Enhancement of motor rehabilitation in multiple sclerosis (MS) patients after Dopamine treatment

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Background It is well established that the metabolism of dopamine in the brain enhances the motor recovery. Besides, no side effects were observed, in mini doses of administration. Because of that, for the period of 3 months we tried the action and the effectiveness of dopamine in patients with MS.
Methods and material We studied the action of levodopa-carbidopa providing with 100mg/d for 3 months vs. placebo 120 patients with definite MS according to MacAlpine criteria. The patients were evaluated according to Kurtzke EDSS and MRI at the beginning and at the end of the treatment. We compared the results of two groups.
Results The group of patients who received dopamine appeared a net improvement of the motor recovery contrary to those who did not receive it.
Conclusion The experience of this study shows a remarkable action of dopamine in the improvement of the motor functions due to MS. This leads to the fact that dopamine, taking into account that it has no side effects, can be administrated as additional medical treatment in MS.

P 3199

Acetyl L-carnitine treatment of fatigue in multiple sclerosis

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Fatigue is a common and disabling symptom of multiple sclerosis (MS). The cause of fatigue is partially known; both peripheral and central mechanisms have been hypothesized. Carnitine is a cellular component exerting a key-role in the energy metabolism control.
Aim of this study was to determine the efficacy of acetyl L-carnitine in MS patients complaining fatigue when compared with amantadine, a drug commonly used to treat fatigue in MS. Thirty-six MS patients with fatigue (21 relapsing-remitting, 15 secondary-progressive) were enrolled into a crossover double-blind treatment program with acetyl L-carnitine (2 gr/die) and amantadine (200 mg/die). Each drug was given for 3 months, with a 3-month washout period. Alternate patients were assigned to be treated with acetyl L-carnitine or amantadine first. All patients were assessed before and after each 3 month-treatment program by using fatigue severity scale (FSS), fatigue impact scale, Beck depression inventory, social experience checklist, and Coop Wonca tables. Changes respects to previous measurements were calculated. Five patients on amantadine and one on acetyl L-carnitine discontinued the treatment due to side effects. In those patients who completed the treatment program, there was a significant improvement in FSS score during the acetyl L-carnitine administration when compared to amantadine intake ($p=0.039$). No significant difference was found in the other clinical scales. Acetyl L-carnitine is better tolerated than amantadine and it results more effective in treating MS-related fatigue. As in chronic fatigue syndrome (CFS), an abnormal carnitine metabolism may be involved in the altered peripheral exercise response observed in MS patients complaining fatigue.

P 3200

IVIg-treatment of experimental autoimmune encephalomyelitis

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Objective Clinical trials have shown that intravenous administration of immunoglobulin (IVIg) has the potential to reduce disease activity in multiple sclerosis (MS). However, the mechanisms by which IVIg interferes with the pathophysiology of MS are not yet fully understood. In the present study, we evaluated IVIg treatment of experimental autoimmune encephalomyelitis (EAE). The objectives of the study were to assess the effects of IVIg on the incidence and severity of active EAE and the EAE pathology in the CNS.
Methods EAE was induced in rats by immunization with spinal cord homogenate. After immunization, animals were treated with infusions of IVIg (1 g/kg) or placebo (10% maltose). The animals were weighed and observed daily, and the clinical disease severity graded on a scale 0–6. At the end of the experiment the animals were sacrificed and the brain and spinal cord dissected and cut for histological examinations.
Results and conclusion Treatment with IVIg significantly suppressed the development of EAE as measured by incidence (placebo 92%, IVIg 50%), day of onset, weight loss and maximal average EAE score (placebo 2.6, IVIg 0.7). In the placebo group, the development of active disease was associated with severe inflammation and demyelination in the CNS. When animals were treated with IVIg, these pathological changes were significantly reduced as measured by the average histological score (placebo 8.8, IVIg 5.3). In conclusion, IVIg treatment of EAE did not simply ameliorate the clinical symptoms of experimental autoimmune disease but had a protective effect against the pathological changes in the CNS.

P 3201

Potential mechanism of action (MOA) of Natalizumab (Antegren™) for multiple sclerosis and other chronic inflammatory diseases

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Introduction Inflammatory foci and demyelination within the central nervous system (CNS) are the hallmark presentation of multiple sclerosis (MS). Integral to this process, leukocyte migration, activation and survival are modulated by the α4 integrins. α4β1 integrin, expressed by circulating leukocytes, mediates their adhesion to VCAM-1, a ligand expressed by vascular endothelial cells at chronic sites of inflammation. Transendothelial migration of leukocytes allows α4 integrin interaction with additional inflammation-associated ligands supporting leukocyte activation. Thus, α4 integrin is an attractive target for treatment of inflammatory diseases; its antagonists represent a new class of agents called selective adhesion molecule (SAM) inhibitors. Natalizumab, a humanized monoclonal antibody against a4 integrin is the first of this class.
Methods In vitro and in vivo studies with natalizumab and its murine antibody precursor (mNat).
Results mNat inhibited human lymphocytes adhesion to VCAM-1 with half maximal inhibition at a concentration of 0.3μg/mL (2nM); complete inhibition at 1μg/mL. Consistent with the known expression pattern of α4 integrin, cytometric analysis documented mNat binding to human lymphocytes and monocytes, and weakly labelled human neutrophils. The affinity of natalizumab and mNat was comparable for guinea pig, primate, and human lymphocytes, with half maximal binding at 0.2μg/mL (K_d=1.3nM). Studies in a guinea pig model of experimental allergic encephalomyelitis demonstrated dose-dependent reversal of disease, including reversal of CNS leukocyte infiltration, hind limb paralysis, cerebral oedema, and blood-brain barrier disruption (measured by MRI).
Conclusion Natalizumab inhibits and reverses inflammation, offering a potential new approach in the treatment of MS and other immune diseases.

P 3202

Differential antigen-specific prevention of experimental autoimmune encephalomyelitis, with naked DNA.

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Introduction Vaccination with naked DNA, by activation of cell-mediated and humoral immune responses, can generate protective immunity against autoimmune diseases, such as experimental autoimmune encephalomyelitis (EAE). We have evaluated the effect of DNA vaccination with plasmids encoding different myelin proteins.
Methods Plasmid vectors, containing proteolipid protein (pvaxPLP) and myelin oligodendrocyte glycoprotein (pvaxMOG) genes, were constructed. We assessed DNA immunization effects on EAE course in SJL/J mice, evoked with PLP (peptide 139–151) and in B6 mice, evoked with MOG (peptide 35–55).
Results The EAE course, in mice immunized with pvaxMOG 4 and 12 weeks prior to EAE induction, was significantly ameliorated. However, in mice immunized with pvaxPLP 4 weeks prior EAE induction, more severe disease was observed and only 12 weeks after DNA vaccination, the EAE course was ameliorated. Prevention of EAE was connected with a decrease in Th1-type cytokine response and in T cell proliferation in both groups of EAE animals.
Conclusion These results indicate that tolerance of EAE with DNA vaccination depends on antigen and/or mouse genetic background.

P 3203

Prospective, randomised, multicentre, assessor-blinded, parallel-group, comparison of the two licensed interferon beta-1a treatment regimens in relapsing-remitting multiple sclerosis

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Introduction/methods The EVIDENCE trial directly compared the efficacy of subcutaneous interferon (IFN) beta-1a (Rebif®), 44mcg three times weekly, with intramuscular IFN beta-1a (Avonex®), 30mcg once weekly, in 677 patients with relapsing-remitting multiple sclerosis.
Results Rebif® demonstrated significant advantages over Avonex® on clinical and magnetic resonance imaging (MRI) endpoints. After 24 weeks, 74.9% of Rebif® patients remained relapse-free versus 63.3% of Avonex® patients (a 32% relative reduction in the proportion of relapsing patients, $p<0.001$). The hazard ratio (HR) for the probability of a relapse on Rebif® compared with Avonex® was 0.63. Rebif® patients had fewer combined unique active lesions (mean 0.7 versus 1.3 with Avonex®, $p<0.001$). At week 48, 96% of patients remained on study, and the treatment effect at week 24 was maintained: the odds ratio was 1.5 ($p=0.009$) and the HR was 0.70 ($p=0.003$). T2 scan results demonstrated that the mean T2 active lesion count per patient per scan was 0.9 (Rebif® group) versus 1.4 (Avonex® group; $p<0.001$) – a 37% relative reduction. The proportion of active scans was reduced in the Rebif® group and 63% (versus 45% in the Avonex® group) demonstrated no MRI activity over 48 weeks. Injection-site reactions (83% vs. 24%), liver (18% vs. 9%) and haematological (11% vs. 5%) adverse events (AEs) were significantly more common in the Rebif® group (but usually mild). There were 17 AE dropouts on Rebif® and 15 on Avonex®.
Conclusions The EVIDENCE trial demonstrated the superiority of Rebif® over Avonex® on MRI lesion activity and the proportion of relapse-free patients.

P 3204

Does the pulsed methylprednisolone therapy influence cognitive functions in patients with multiple sclerosis?

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Introduction Treatment with high-dose glucocorticoids is a well established therapy in multiple sclerosis (MS), but only little is known about the side effects on cognitive functions.
Methods We studied sixteen patients (11 females, 5 males; mean age 33+/–9.34 years) with relapsing-remitting MS in early disease stage treated for a relapse and eight healthy controls matched for age, gender and IQ clinically and neuropsychologically. To detect dose-dependent effects, one half of the patients were treated with 500-mg/d methylprednisolone (MP) over five days, the other half received 2000 mg/d MP. Neuropsychological investigations were made before (day 0) and at day 6 and day 60 after starting the therapy.

Results Results show significant deficits of free and cued retrieval of declarative memory in the patients at day 6 compared to day 0. These cognitive deficits recovered completely at day 60. All other functions were unaffected. In contrast, the untreated controls showed a slightly improvement in their declarative memory at day 6. No differences were found between the profile and severity of the cognitive impairment of the two dose groups.
Conclusion The findings suggest that high-dose treatment with MP may be associated with selective, but reversible impairment of the declarative memory-recall in MS patients. There may be no association to the administered MP dose.

P 3205

Impairment and driving performance in relapsing remitting multiple sclerosis

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Introduction Different deficits may influence driving capacity in relapsing-remitting multiple sclerosis (RRMS). Our study compared driving simulator performance with fatigue, physical and cognitive functions in RRMS.
Methods 31 RRMS patients (18 women, 13 men, mean age 35.6±8.3 years) and 19 healthy controls (9 men, 1 woman, age: 55.1+7.8 years) were assessed by:
– Extended Disability Status Scale (EDSS)
– MS Functional Composite (MSFC) based on arm function, ambulation and cognition (paced auditory serial addition test, PASAT).
– Fatigue Severity Scale (FSS)
– Driving simulator: Driving on a highway for 60 minutes (mean speed 100 km/h). Presentation of a monotonous condition with different weather and daytime conditions. Obstacles occurred infrequently.
Results FSS - Score was raised with intra-individual variability (38.5±15.5). FSS correlated with arm function ($r=0.465$) and ambulation ($r=0.436$) in the MSFC ($p<0.05$). Compared to controls accident rate (5.3±3.8 vs. 1.3±1.5, $p<0.001$) and concentration faults (21.1±15.5 vs. 7.1±2.6, $p<0.01$) of RRMS patients in the driving simulator were increased. MSFC correlated with accident rate ($r:-0.5$, $p<0.05$). Correlation depended on cognitive function measured by the PASAT($r:-0.33$, $p<0.05$).
Conclusion Impaired driving skills in RRMS could be demonstrated. In the MSFC, most patients showed cognitive deficits. Correlation of PASAT and driving simulator accidents indicated that accidents are more influenced by cognitive decline than by physical impairment. The driving simulator seems to be the best instrument for judging driving ability.

P 3206

Multiple sclerosis patients with autoimmune thyroiditis have a worse disease course

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Introduction There is no report concerning the course of multiple sclerosis (MS) in patients with co-existing autoimmune thyroiditis (AIT). Thyroid hormones are essential for normal brain development and myelination and therefore might influence remyelination in MS. Moreover, thyroid hormones influence the differentiation of oligodendrocyte precursor cells.
Methods We included 92 patients (68 women and 24 men) with definite relapsing-remitting MS and examined the thyroid gland and the disability status via the expanded disability status scale (EDSS) every three months during a prospective three-year surveillance. Thyroid examination included: clinical and ultrasound investigation, detection of thyroid hormones and antithyroid antibodies. The EDSS-examiner was blinded with regard to thyroid disease. All patients lived about 100 km around the hospital and therefore had a comparable iodine intake.
Results The patients with AIT showed a clearly worse disease course as shown by EDSS. No severe thyroid dysfunction could be observed.
Conclusion The co-existence of another organ-specific autoimmune disease with MS obviously accelerates the progression of disability.

P 3207

Epidemiological and clinical aspects of multiple sclerosis (MS) in Tunisia

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Background Prevalence of MS was considered to be low in Tunisia. The use of MRI criteria allows earlier diagnosis and the use of Kurtzke scale for disability allows a better management.
Patients and Methods Among 1058 records of patients classified MS and followed in our department between 1974 and 2000, we selected two groups of patients belonging to two periods differing in the diagnosis tools and the type of management: group I (1974–1978, 125 patients classified according to Mac Alpine criteria) and group II (1996–2000, 247 patients classified according to Poser's criteria). The two groups of patients were compared for clinical and paraclinical parameters and outcome.
Results The prevalence of the disease was similar over the 2 periods and higher than expected for a low prevalence zone. Age of onset was 32.4±10.1 years, delay between the onset of the disease and diagnosis was 3.8±4.4 years and mean disease duration was 6.2±6.7 years. Most patients (72.6%) had relapsing-remitting MS. Most frequent symptoms of onset were motor (53.5%), sensory (42.7%) and visual (32.8%). MRI allowed earlier diagnosis in group II as compared to group I. Systematic treatment with methylprednisolone in patients of the group II shortened the duration of relapses but did not influence the final disability.
Conclusion Tunisia is a medium prevalence zone for MS. The use of MRI allowed earlier diagnosis of paucisymptomatic forms of MS but did not increase the overall proportion of definite MS.

P 3208

Co-incidence of multiple sclerosis and immune thrombocytopenic purpura (a case report)

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Background Multiple sclerosis (MS) and immune thrombocytopenic purpura (ITP) are immunologic diseases of which the aetiologies are unknown.
Report of case A 17-year-old girl was referred to neurology clinic because of diplopia since 4 days. She had a history of ITP from 5 years ago. In examination, we find right side inter-

neuclear ophthalmoplegia. Other examinations were normal. Brain MRI showed multiple hyperintense lesions around lateral ventricles and one in pons. Right side VEP was abnormal. Brain stem and somatosensory evoked potentials were normal. Cerebrospinal fluid was normal. Blood count was normal except thrombocytopenia.
This patient had been treated by methyl prednisolone 1000 mg/day for 5 days and then 50 mg prednisolone orally for 10 days. After 3 days, she felt better and her diplopia had disappeared. About 4 months later, she noticed ataxia and right side weakness. Platelet counts were lower than normal again. MRI revealed new plaques in her cerebellum and brain stem. After repeated pulse therapy, Beta Interferron 1b (betaseron) was started. Now she has been okay and under control for 22 months but her neurological problem and thrombocytopenia are bothering her every now and then.
Conclusion Neurological autoimmune disorder such as MS, Myasthenia Gravis, etc, may accompany some other diseases. This may be due to genetic susceptibility or any unknown aetiologies, but accompanying MS and ITP is a rare condition. In our investigation, we could not find any other cases like this in her family. Good response to immunomodulator treatments suggest autoimmune basis for the aetiology.

P 3209

Reduced functional and respiratory parameters in multiple sclerosis and the relation to fatigue

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We have monitored functional and respiratory parameters in multiple sclerosis (MS) and tried to find their relation to fatigue. 54 MS outpatients were studied. Disability was evaluated according to expanded disability status scale. Fatigue, according to modified fatigue impact scale. Respiratory parameters on Spiro meter, by flow/volume method. Functional parameters were evaluated on bicycle spiroergometer using the anaerobic threshold method. Obtained values were compared with the norm, and statistical analyses were carried out using Statistical Analysis System.
14 of the subjects were men, mean age of subjects was 37.03±10.1 years, disability 2.8±1.53, and illness duration 8.33±6.62. Maximal functional parameters W/kg, HR, VE/kg, MET, VO2/kg/ml, BF, VTex ($p<0.001$), O2HR ($p<0.05$) and respiratory parameters PEF ($p<0.001$), MEF75, 50, 25 ($p<0.05$) were significantly lower. RQ, EqO2, EqCO2 VCin, VCex, ERV, FVC, FEV1 corresponded to the norm. Fatigue increases significantly with increasing degree of disability ($p<0.05$), further with age and duration of the illness ($p<0.1$). However, it decreases significantly with relative weight ($p<0.1$). We found an important correlation between fatigue and respiratory parameters METS ($p<0.001$), VTex, HR, VO2/kg/ml, O2HR ($p<0.05$), W/kg, VE/kg ($p<0.1$). We did not find any correlation between fatigue and respiratory parameters, even though a larger percentage of the patients (78%) complained of dyspnoea.
Even in people with relatively low degree of disability cardiovascular fitness is reduced. It decreases with disability and the duration of the illness as well, and participates in the genesis of fatigue. Significantly, decreased values of the expiratory flow, which may reflect muscle weakness, do not participate in the genesis of fatigue.

P 3210

Lower urinary tract dysfunction in patients with multiple sclerosis.

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Objective The lower urinary tract (LUT) symptoms are common in multiple sclerosis (MS) patients and may be main cause of social disability.
The **aim** of the study was assessment frequency and nature of LUT dysfunction in MS population and their impact on quality of life.
Materials and method 60 consecutive MS patients were included (mean age 42.2; mean duration of disease 13.1; mean age of MS onset 28). 65% of patients were female.
The symptoms were assessed with multiplane questionnaire: A list of symptoms and signs, "obstructive" and "irritative" scores (International Prostate Symptom Score (IPSS), Boyarsky, Madsen), and patient self-assessment of the quality of life (QOL). Functional bladder capacity and the post-void residual urine volume (PVR) were measured ultrasonographycally.
Results In 5% of patients, LUT symptoms were the first manifestation of the disease. LUT dysfunction occurred in 93.3% of patients: frequency 63.3%, nocturia 61.6%, urgency 43.3%, hesitancy 48.3%, interrupted urinary flow 41.6%, sensation of incomplete emptying 48.3%, incontinence 48.3%, in 28% PVR was over 100ml. The intensity of LUT symptoms correlate well with EDDS, lower limbs paraparesis, results of QOL and scores ($r=0.65-0.78$; $p<0.05$). Before study inclusion, only 15% of patients were pharmacologically treated and few were treated with physiotherapy
Conclusions Urological disturbances occur in most patients with MS, careful diagnostic procedure should be performed for each patient. Appropriate management strategies are needed to improve the function and quality of the patient's life.

P 3211

Injuries in the pathogenesis of multiple sclerosis

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Background and purpose An injury might derange the protective function of the blood-brain barrier, and thus it represents one of the possible pathogenetic factors in the demyelination of the neural axis. However, the effect of injury on the occurrence or deterioration of multiple sclerosis (MS) is still controversial.
Methods In this research, for every MS patient there was a randomly chosen control patient/subject of same gender, same birthplace and place of residence.
These control study subjects could have been diagnosed with any other illness except MS, other illnesses of known immunocauses or mental illness.
In this research, we used the statistical methods "case-control" studies.
Results In three patients following multi-traumatic injuries or serious head injuries, which followed after being diagnosed with MS, there was a worsened state.
Conclusion According to most authors, the importance of injury in individual cases of MS is undeniable, as well as the fact that injuries are factors of progression and deterioration of the disease, but never its cause. Consequently, injuries can cause only temporary disability, and not permanent. Nevertheless, the

incidence of MS increases proportionally to the severity of injury. The length of the period from the occurrence of injury to possible demyelination is still not established. Studies and clinical reports point to the fact that in the evaluation of injury as a precipitating factor for the vulnerability of the blood-brain barrier, the severity of the injury is of greater importance than its site.

P 3212

Fatigue in patients with multiple sclerosis: relationship to disease pattern, disability, and depression

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The symptom of fatigue is a frequent complaint in multiple sclerosis (MS) patients.
The **aim** of this study was to determine the link between fatigue and clinical features of MS and evaluate the specificity of three fatigue scales in this condition.
109 individuals with clinically definite MS: relapsing-remitting 79 (72.5%), secondary progressive MS 17 (15.6%), and primary progressive 13 (11.9%). Mean disease duration was 8.3 years. Mean EDSS score was 4.2 (range 1.0–8.0). Fatigue was measured using the Fatigue Descriptive Scale (FDS), Fatigue Severity Scale (FSS), and Visual Analogue Scale (VAS).
Fatigue was present in 92% of MS patients. The global FDS score was 5.0+2.6 (range 1–13), FSS was 5.2+1.5 (range 1.5–10) and VAS was 58.8+22.4 (range 10–100). FDS and FSS were highly correlated ($r=0.61$, $p<0.0001$). Patients with progressive MS had higher fatigue score than relapsing remitting MS patients, but the difference was not significant ($p=0.247$). FSS and FDS scores no longer correlate with EDSS ($r=0.27$, $p=0.09$). Patients with MS experienced significant fatigue not related to depression ($r=-0.087$, $p=0.385$).
Our **results** supports the notions that fatigue is very frequently present in MS and suggest that it is not related to affective disturbance and neurological impairment in these patients.

P 3213

Schilder's myelinoclastic diffuse sclerosis – a case report

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Introduction Schilder's myelinoclastic diffuse sclerosis, a variant of multiple sclerosis, is a very rare disease that occurs in children and adults. It is usually presenting as an intracranial mass lesion.
Case report The 49-year female patient was referred to our hospital with progressive right-sided hemi paresis, motor dysphasia and frontal lobe syndrome. Symptoms started 14 days earlier with acute headache. Febrile state was not examined. MRI of the head revealed two oval lesions with hyper intensity in T2 weighted images of left frontal and parietal lobe. The first diagnostic impression was of glioblastoma multiform. Analysis of CSF revealed increased immunoglobulins, 3 OCB and increased intrathecal synthesis of IgG. The biopsy after neurosurgical stereotactic treatment yielded five needle cores of greyish tissue. Haematoxylin and eosin stained sections of paraffin embedded tissue showed cerebral white mater infiltrated by large numbers of Luxol fast blue negative, lipid containing macrophage which were CD 68 immuno-positive. Enlarged number of astrocytes was also present. Some of them contained granulated nucleus like sign of mitosis. Proliferating cell nuclear antigen (PCNA) and Ki67 indicated that these cells proliferated. Fragmenting myelin sheaths were present at the relatively sharp edge of inflammatory lesion. Perivascular cuffing by CD3 and CD 20 lymphocytes were scant. Silver impregnation and immunocytochemical reaction with monoclonal antibodies to neurofilaments indicated that in demyelinating lesions network of axons was preserved.
Conclusion Pathohistological findings are consistent with the diagnosis of Schilder's myelinoclastic diffuse sclerosis.

P 3214

First demyelinating syndrome and risk of progression to multiple sclerosis in Chinese patients

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Objectives To study the clinical, cerebrospinal fluid (CSF), and radiological findings in Chinese patients with first demyelinating syndrome and the risk of progression to multiple sclerosis.
Methods All patients presenting with first demyelinating syndrome to our unit over the period 1993 to 2001 were included. The hospital records were retrospectively reviewed and data on clinical features, CSF findings and MRI of the brain and/or spinal cord were systemically analysed. The progression to multiple sclerosis and the associated risk factors were also studied.
Results Twenty-seven patients with first demyelinating syndrome were identified over the study period of 105 months: eighteen were females and mean age 43.2 years. The syndromes were: transverse myelitis (66.7%), optic neuritis (25.9%) and brainstem syndrome (7.4%). Eleven percent (3/27) of patients with transverse myelitis had concomitant optic neuritis on evoked potential study. Oligoclonal bands were positive in 25% (3/12) of patients. MRI showed the corresponding lesion in 76% (19/25) and 36% (9/25) had additional lesion in other sites. One patient died, four had recovery with significant deficit, and twenty-two had good recovery. The treatment with pulse methylprednisolone was associated with good outcomes (complete recovery) in 16/19 versus 3/8 patients. After a mean follow up of 29 months (range 5 to 84 months), 8 patients (25.5%) progressed to multiple sclerosis. The associated factor identified was high lesion load on MRI.
Conclusion In Chinese transverse myelitis is the most common presentation for demyelinating disease. The prevalence and risk of progression to MS is lower than that of Caucasians.

P 3215

Management of co-ordination disorders in multiple sclerosis patients.

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Co-ordination and vestibular disorders lead to malfunction problems in 60–70% multiple sclerosis (MS) patients. There is still no specific pharmaceutical management of such conditions. The **aim** of this research has been to develop a vestibular-training programme to counteract various types of ataxia in patients with MS. The vestibular-training programme has been introduced to a group of 19 patients (18–42 years old, 12 female, 7 male). Average duration of the disease was 8.2±1.4 years. All patients displayed moderate symptoms of dynamic and static ataxia. A control group included ten patients with no

vestibular training form. Three principle VT schemes, combined with biofeedback method, were used for managing the following symptoms: 1) dynamic ataxia 2) static ataxia 3) vestibular-sensor disturbances. Vestibular-sensor, vegetal reactions and coordination tests were conducted. The rehabilitation indices in the MS patients receiving VT were significantly better. It is believed that the VT method serves to engage new interneuronal links and thus reduce coordination disorders.

P 3216

An erythromelalgia case occurred during interferon beta treatment for multiple sclerosis

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Introduction Common side effects of the interferon beta (IFNB) therapy include flu-like symptoms, skin reactions at the injection sites, leukopenia and raised concentrations of liver enzymes. In addition, of these well-known side effects, vascular complications associated with IFNB have also been, although rare, reported. Nevertheless, erythromelalgia related to the IFNB beta treatment has not yet been encountered. We report the first erythromelalgia case occurred during the interferon beta-1a (IFNB-1a) treatment for multiple sclerosis.
Case reports A 38-year-old woman who had been treated with IFNB-1a for relapsing remitting multiple sclerosis for 20 months was evaluated with the complaints of burning pain, elevated temperature and dermal erythema in feet. She described relieving of the pain with elevation of the lower extremities and cold exposure. She was diagnosed as having erythromelalgia and secondary causes were investigated. After excluding all possible causes, erythromelalgia in this case was thought to be associated with IFNB-1a treatment and the drug was discontinued. Following the withdrawal of the IFNB-1a, the symptoms and signs recovered gradually and disappeared completely at the end of 15th day.
Conclusions Erythromelalgia as a result of IFNB has not been reported in literature. The present case is believed to be the first report about the association of erythromelalgia with IFNB.

P 3217

Effect of glatiramer acetate(Copaxone) on the level of IL-10 and IL-12 in multiple sclerosis

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Introduction Proinflammatory cytokines produced by Th-1 cells and cytokines with immunosuppressive properties play on important role in the pathogenesis of multiple sclerosis (MS). Glatiramer acetate (GA) is one of the most important immunomodulatory agent used in the therapy of MS. The mechanism of action of GA in MS is not yet fully explained. The purpose of this study was to evaluate the effect of GA in a dose 20 mg daily in a period of 6 months on interleukins IL-10 and IL-12.
Methods Thirty-one patients with definite MS and 30 control subjects were the subjects of our study. The ELISA measured the interleukin levels in sera.
Results A significant increase was found of IL-12 and also of IL-10 levels in MS patients in comparison with control groups. We have also established a significant decrease of IL-12 after 3 and 6 months of GA therapy and some insignificant differences in the level of IL-10.
Conclusion IL-12 seems to contribute to the pathogenesis of MS. The established down regulation of IL-12 suggest down regulatory action of GA on IL-12.
The insignificant change of IL-10 level observed in course of GA therapy seems to indicate that this cytokine is not connected with the immunomodulatory effect of GA in MS.

P 3218

4-year clinical experience with interferon beta 1b in relapsing-remitting multiple sclerosis patients

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Introduction The benefit of interferon beta was shown to decrease the clinical and MR activities of multiple sclerosis (MS) in several large studies. We wanted to obtain a feedback from the everyday practice with interferon beta in our MS Centre.
Methods In the retrospective study, we selected 55 patients with relapse-remitting multiple sclerosis started on the first interferon beta available in the Czech Republic since 1996.
Results The relapse rate tremendously declined from 1.87 in 2-year pre-treatment period to 0.43 in the first year of treatment. Thereafter it remained relatively stable for the following 3 years (0.4, 0.2, 0.3, respectively). Clinical disability preserved unchanged ranging from 2.4 to 2.7 through the period analysed. 25% of patients, 20% of patients were relapse-free after 2, 3 years, respectively. Five patients failed to respond. 21% of patients exhibited necrosis.
Discussion The overall clinical efficiency in our group was found to be higher than in classical Betaferon studies due to several reasons. The study design was obviously different. The candidates eligible for interferon therapy were strictly selected, especially according to the high activity of the disease before interferon treatment. Moreover, we usually combine disease-modifying therapy with corticosteroids or immunosuppressive drug that may reduce further a CNS inflammation. Higher frequency of necrosis was probably caused by the inappropriate injection procedure, since this adverse event has been reduced by auto injectors' introduction nowadays.
Conclusion Combination therapy is more effective than isolated interferon treatment only.

P 3219

Effects of a cooling suit in multiple sclerosis

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Introduction Personal cooling systems are used to alleviate symptoms of multiple sclerosis (MS) with great success. Recently a portable cooling suit and a cooling helmet were constructed to cool head and neck regions of patients with MS, but little scientific work has been done on these types of suits.
Methods As part of a retrospective study, 30 females and 20 males aged 18–65 years were interviewed by telephone. All of the subjects were asked the following: Where there any subjective changes in the movement of legs or arms, in eyesight, in

feeling of energy, in pain, mood, fitness or cognitive ability after the treatment with the cooling suit and helmet, how long did they feel better and was the cooling system pleasant.
Most of the subjects had a progressive course of MS and stated that they were heat sensitive.
Results In 94 percent of patients the cooling therapy was pleasant, no one took a turn for the worse. An unexpected result was found in 12%. These subjects could see better and one third of all subjects had more control over their muscular movements after 30 minutes of the cooling period.
Regarding the mobility and nicotine-consumption only 27% of smokers but 40% of non-smokers indicated improvement.
In our spot check, more subjects with normal cholesterol levels felt better, than patients with pathologic cholesterol levels.
Conclusions These results show that the cooling suit seems to be an effective method for improving the eyesight and mobility of MS patients.

P 3220

Clinical and immunological monitoring in secondary progressive multiple sclerosis (SPMS) patients during transcranial magnetic stimulation (TMS).

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P 3221

Therapeutic aspects of multiple sclerosis at the neurology clinic of clinical centre of Sarajevo University

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P 3222

The epidemiology of multiple sclerosis in Devon: A comparison of the new and old classification criteria

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Multiple sclerosis (MS) is the most common cause of neurological disability in young adults in the United Kingdom (UK). There is significant variation in the worldwide distribution of MS and it remains debatable as to whether a latitudinal gradient exists across the UK. We present the first epidemiological study of MS to be conducted in Devon. With its low latitude and relatively low migration rates it is an ideal region to be studied and compared with the north of the UK.
A population-based survey was carried out using seven sources (neurology department, hospital episode statistics, MS specialist nurse, MS society, regional residential/nursing homes and general practitioners). Hospital notes were inspected to ensure accurate diagnosis and cases were classified according to both the Poser criteria and the new McDonald criteria. We report a crude prevalence of 118 per 100,000 (Poser criteria) in a population of 341,796, on prevalence day 1st June 2001.
This study provides the first prevalence figure for this part of the UK, as well as being the first to use the new diagnostic guidelines and compare them with the Poser criteria. Age-sex standardisation was used to allow for the demographic structure of the population. This figure is one of the highest reported in the south of the UK and provides further support for a north-south divide, indicating that this is a step effect rather than a direct latitudinal gradient.

P 3223

The effect of oral cannabis oil on tremor in patients with multiple sclerosis

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Introduction Tremor is a common symptom in patients with multiple sclerosis. Anecdotal evidence suggests that some such patients find relief by using cannabis. However, no previous randomised controlled trials of cannabis as a treatment for tremor have been performed.
Methods We carried out a randomised double blind placebo controlled crossover trial of oral cannador (cannabis oil) in 14 patients with multiple sclerosis and significant tremor. Patients received each treatment for a period of two weeks before assessment of effect. The primary outcome measure was improvement on a 0 to 10 clinical rating scale of tremor, with secondary outcome measures including accelerometry, spiral drawing, finger tapping and nine-hole peg board.
Results There was no significant improvement in any of the objective outcome measures. Despite this, more patients reported subjective improvement in their tremor when given cannador (5 out of 14) than when given placebo (1 out of 14).
Discussion The trial was powered to detect an improvement in tremor of 50%, which was felt to be the minimum which would be clinically significant. The absence of any significant result suggests that, despite anecdotal reports, cannabis cannot be considered an effective treatment for tremor secondary to multiple sclerosis.

History of neurology

P 3224

Erasmus Darwin (1731–1802), Neurologist

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Erasmus Darwin was a foremost physician, scientist and poet during the latter years of the eighteenth Century. He wrote extensively and his poetry included three long works which advanced many of the ideas subsequently attributed to his grandson, Charles Darwin, who became very well known for his work *On the Origin of Species*.
Erasmus Darwin's works included reference to many topics now regarded as the province of neuroscience and among these are the development of the nervous system, porphyria, compression therapy of the brain, colour vision, after-images, visual memory, the demonstration of the blind spot, aspirin, and curiously his thoughts about the brain and muscles of vegetables.