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Epilepsy

SC 301

MR-volumetry of subcortical structures in temporal and extratemporal epilepsy

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Introduction Animal and human data suggest a crucial role for subcortical structures in the modulation of seizure activity, mostly as seizure-suppressing relays. There is, however, little knowledge about the actual size of implicated subcortical structures in epilepsy patients.
Method Using high-resolution MRI, we measured the volumes of subcortical nuclei, such as the thalamus, caudate nucleus, putamen and pallidum, in both hemispheres of 27 patients with temporal lobe epilepsy (TLE) and 31 patients with extratemporal lobe epilepsy (ETLE). ETLE patients were further subdivided in patients with a left and right anterior, left and right posterior focus. 16 volunteers served as controls.
Results Compared to the control group, TLE patients showed significantly smaller striatal and thalamic volumes, predominantly on the ipsilateral side ($p<.01$). In contrast, ETLE patients as a whole did not differ from the control group. However,

ETLE subgroups (with respect to focus localization) differed with respect to thalamic volumes.
Conclusion Volumetric measurements of subcortical nuclei revealed significant atrophy of distinct subcortical nuclei in the TLE group, but not in the ETLE group. Our findings suggest that TLE and ETLE represent different entities also on the subcortical level. Differences of the focus localization in the ETLE group were reflected in different sizes of thalamic nuclei. A distinct pattern of subcortical atrophy is of particular interest with respect to development of alternative treatments.

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Low-frequency rTMS in patients with cortical dysplasia

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Introduction Epilepsy is associated with cortical hyperexcitability. Low frequency repetitive TMS (rTMS) can decrease cortical excitability. Recently data have been provided about the potential therapeutic role of rTMS in intractable epilepsy (Tergau et al., 1999). The aim of this study was to investigate the effects of focal low-frequency rTMS in refractory epilepsy due to cortical dysplasia.
Method We treated 4 patients (1 M, 3 F mean age 29.5±2.6, range 27–33 years) with refractory seizures due to cortical dysplasia (2 with single and 2 with multiple foci) at EEG and NMR imaging. 8 rTMS sessions were given biweekly for 4 weeks. Each session consisted of one train of 100 pulses at 0.5 Hz at 90% of motor threshold over the area of cortical dysplasia in the 2 patients with a single focus and over the vertex in the other 2.The number of seizures during the month before stimulation (time I) were compared by repeated measures ANOVA with that of the month during (time II) and after stimulation (time III).
Results rTMS significantly reduced the number and severity of seizures in patients with a single dysplasic focus (main effect of time: $F(2.3)=21.50$; $p<0.01$). The improvement concerned predominantly the disappearance of secondary generalization and was still persistent one month after the end of the treatment: (time I vs II, time I vs III: $p<0.001$ at post-hoc).
Conclusion Our results show that a long-lasting depression of cortical dysplasic area may temporarily improve intractable epilepsy.

SC 303

The antiepileptic drug levetiracetam reverses the inhibition by negative allosteric modulators of neuronal GABA- and glycine-gated currents

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Introduction In this study in vitro and in vivo approaches were combined in order to investigate if the antiepileptic mechanism(s) of action of levetiracetam (LEV; Keppra®) may involve modulation of inhibitory neurotransmission.
Method GABA- and glycine-gated currents were studied in vitro using whole-cell patch-clamp techniques applied on cultured hippocampal, cerebellar granule and spinal neurons. Protection against clonic convulsions was assessed in vivo in sound susceptible mice. The effect of LEV was compared with the AEDs carbamazepine (CBZ), phenytoin (PHT), valproate (VPA), clonazepam (CZP), phenobarbital (PB) and ethosuximide (ESM).
Results LEV contrasted the reference AEDs by an absence of any direct effect on glycine-gated currents. At high concentrations, beyond therapeutic relevance, it induced a small reduction in the peak amplitude and a prolongation of the decay phase of GABA-gated currents. A similar action on GABA-elicited currents was observed with the reference AEDs, except ESM. These minor direct effects contrasted with a potent ability of LEV (EC50=1–10:M) to reverse the inhibitory effects of the negative allosteric modulators zinc and b-carbolines on both $GABA_A$ and glycine receptor-mediated responses. This pharmacological profile was not mimicked – or only partially – by the reference AEDs. Likewise, co-administration of β-carbolines, but not flumazenil, abolished the seizure protection afforded by LEV (17 mg/kg, i.p.).
Conclusion The results of the present study suggest that a novel ability to oppose the action of negative modulators on the two main inhibitory ionotropic receptors may be of relevance for the antiepileptic mechanism(s) of action of LEV.

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Acute treatment of experimental status epilepticus with levetiracetam reduces chronic spontaneous recurrent seizures

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Introduction Levetiracetam (LEV) is very effective in the acute treatment of experimental status epilepticus (SE). We report its efficacy in reducing the long-term consequences of SE in an animal model of self-sustaining SE.
Method SE was induced by perforant path stimulation (PPS) for 30 mins in awake animals then LEV was injected iv. Seizures and spikes were recorded for 24 hours during SE, ≥ one week 1–2 months later, and analysed using Harmonie software.
Results I.v. administration of LEV 10 mins after PPS attenuated SSSE, reducing cumulative seizure time from control 606±57 to 22±96, 18±5 and 9±2 mins for LEV 200, 500, 1000 mg/kg respectively ($p<0.05$). At 40 mins, LEV reduced serum neuron-specific enolase (NSE), (26.8±3U to 8.2±2.1U) similar to controls (5.4±0.4U), suggesting a marked reduction in seizure-induced neuronal death. All control rats developed recurrent spontaneous seizures (SRS) 28±2 days after SE. Seizure frequency remained stable over the next 50 days (dl: 6±1; d10 8±1; d30 7±1; d50 7±1). LEV 200 mg/kg treated rats had SRS 31±1 days after SE, seizure frequency was only 1 (d1) or 0.5/day (d10, 30, 50). After LEV 1000 mg/kg, SRS were absent (50% rats) or infrequent.
Conclusion These results suggest acute treatment of experimental SE with LEV to reduce both incidence and severity of its chronic consequences.
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Tolerability of levetiracetam in a population of older patients with cognitive and anxiety disorders

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Introduction The purpose of our study was to review the tolerability of levetiracetam (LEV) in a population of older patients (≥65 years) diagnosed with a cognitive or anxiety disorder.
Method LEV was evaluated in placebo-controlled, monotherapy trials that included 738 patients with Cognitive Disorders, of whom 319 were ≥65 years, and 1,609 patients with Anxiety Disorders, of whom 169 were ≥65 years. Data are reported as comparison of the incidence of specific adverse effects in the LEV and placebo groups (where the incidence was ≥5% in the LEV group).
Results Common problems in the Cognitive group were asthenia (7.1%), somnolence (4.5%), urinary tract infection (4.1%), dizziness (3.3%), and headache (1.3%). Common problems in the Anxiety group were headache and tremor (5.2%), urinary tract infection (4.1%), weight loss (4.0%), anorexia, pharyngitis, and abdominal pain (3.8%), insomnia (3.0%), vomiting (2.4%), and oedema (2.0%). In comparison, the younger group of patients with epilepsy who received LEV reported somnolence (6.4%), infection (5.9%), asthenia (5.6%), dizziness (4.7%), pharyngitis (2.2%), and pain (0.7%). The type and incidence of adverse effects reported by older patients were lower than reports from the predominantly younger epilepsy patients taking multiple AEDs.
Conclusion LEV was well tolerated by older patients with central nervous system disorders other than epilepsy. No problems occurred among these older patients that were not seen in the epilepsy population, nor were the rates higher. These data indicate that adverse effects associated with LEV were minimized when the drug was used as monotherapy, even in this vulnerable population.

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Seizures (Sz) after ischemic stroke (IS): a 2-year prospective study

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Introduction The purpose of our study was to analyse the frequency and risk factors (RF) of early seizures (ES) and late-onset seizures (LS).
Method All patients with IS admitted to neurological clinic between September 1, 1997 and April 1, 1998 were followed up for 2 years or until death.
Results The cohort consisted of 328 patients. Sz occurred in 32 (9.75%), ES – in 20 (6.1%), LS – in 18 patients; 30% of patients with ES subsequently had LS. In the univariate analysis significant differences between patients with and without ES were found for: age 70 – 79, moderate severity of stroke, hypertension, atrial fibrillation (AF). ES were associated with recurrent stroke (RS) and severe/moderate deficit in the late restoration period. With multiple logistic regression, AF was a significant RF for ES, and ES were a strong predictive factor for RS. 20% of patients with ES died during the first month of stroke compared to 8.4% of patients without ES. Cumulative risk of LS was 3.27% at 1 year and 5.70% at 2 years. In the univariate analysis significant RF for LS were: age 50 – 59, mild/moderate stroke, AF, and smoking. With multivariate analysis, only AF was a significant RF for LS.
Conclusion ES occurred in 6.1% of IS patients. Only AF was a significant RF for ES, while ES were a strong predictive factor for RS and LS. Cumulative risk of LS was 5.7% after 2 years of stroke.

Ageing and dementia 2

SC 307

Age-related white matter changes as a predictor of disability in the elderly: The LADIS (Leukoaraiosis and DISability) project

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Introduction Age-related White Matter Changes (ARWMC) as detected by brain imaging are associated with cognitive, motor, mood, and behaviour disturbances, all conditions related to disability in the elderly. The LADIS (Leukoaraiosis And DISability) project is a Concerted Action supported by the European union within the V Framework Program. 13 European centres collaborate with the aim to evaluate ARWMC as independent determinant of transition to disability in the elderly.
Method 800 subjects/patients aged 65 – 84 with ARWMC of different severity and no/mild disability, will be enrolled in 4 settings (stroke, dementia, geriatrics, population), assessed at baseline, and followed-up for 3 years. Subjects will be evaluated at baseline with standard clinical and functional tests (including tests for cognitive and motor functions and tests for depression). These tests will be repeated yearly for 3 years. MRI study is performed at baseline and repeated at the end of the follow-up in order to evaluate the progression ARWMC.
Results Outcome events including death, dementia, stroke, and depression will be registered. The relative risk of transition to disability and the risks of death, dementia, stroke, and depression will be estimated in the 3 severity ARWMC groups adjusting for other determinants of disability. Transnational harmonization of clinical and MRI assessments of ARWMC are ongoing and will be a further deliverable from this collaborative project.
Conclusion Clinical and radiological data will serve for identifying strategies for preventing and treating ARWMC thus contributing to reduce the burden of dependent aging in Europe.

SC 308

Detecting mild cognitive impairment (MCI) patients with the DemTect®

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Introduction The DemTect®, a new screening instrument (Kessler et al., 2000), consists of five subtests: word list learning, number transcoding, digit span (reverse), supermarket task, and delayed recall of the word list. The following cognitive domains are assessed: verbal short- and long-term memory, number processing, language, working memory, cognitive flexibility, and speed of information processing. This study repre-

sents a comparison of the performance of healthy control subjects (CG) with patients with mild cognitive impairment (MCI) on the DemTect® subtests.
Method 99 subjects were enrolled. 38 had a diagnosis of MCI, without dementia. The remaining 61 participants were healthy control subjects without cognitive impairment (CG). Both groups were comparable in age: MCI, 74.91 (SD=5.79) years; CG, 74.81 (SD=6.31) years. The MMSE score of the MCI group was 27.76 (SD=1.13), versus 27.91 (SD=1.74) in the CG. This difference was not statistically significant.
Results The MCI group demonstrated significantly lower ($P<0.01$–$P<0.001$) scores on all five DemTect® subtests than the CG (MCI vs CG: word list 9.01 vs 11.3; transcoding 3.1 vs 3.73; verbal fluency [supermarket task] 14.5 vs 22.90; digit span 4.3 vs 4.98; delayed recall 1.6 vs 3.3).
Conclusion In contrast to the MMSE, the DemTect® is a very useful tool for the identification of patients with mild cognitive impairment. The sensitivity of the DemTect® over the MMSE reveals that MCI patients may have cognitive deficits in addition to impaired memory.
Literature
Kessler J, Calabrese P, Kalbe E, Berger F (2000). DemTect: Ein neues Screening-Verfahren zur Unterstützung der Demenzdiagnostik. Psycho; 26:343–347.

SC 309

Anosognosia in mild Alzheimer's disease: revelations by FDG-PET

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Introduction We examined regional cerebral glucose uptake in mild AD patients, who, in addition, exhibited anosognosia (lack of awareness of symptoms). FDG-PET was utilized by using a new cognitive stressor, the Emotional Counting Stroop Test (ECS). Previous studies suggest that the Stroop Test evokes selective attention, which is believed to be mediated by the Anterior Cingulate Cortex (ACC) (Posner, 1996).
Method 10 mild AD patients were selected based on the MMSE score between 20 and 24. The FDG-PET scans were performed 20 minutes after undergoing the ECS, a cognitive task specialized for functional neuroimaging. A baseline PET scan and the Anosognosia Questionnaire (a questionnaire developed to objectively evaluate anosognosia in AD) were administered on separate occasions. Quantitative image subtraction was done using SPM99 software.
The co-registration of PET images with the patients' MRI scans was performed to more accurately identify areas of altered glucose metabolism.
Results 6 patients exhibited anosognosia as identified by the Anosognosia Questionnaire. A significant loss of inferior ACC and right posterior parietal glucose uptake was identified in 5 of the 6 anosognosic AD patients ($p<.01$). The magnitude of the glucose uptake loss in the ACC correlated positively with anosognosia score in mild AD ($p<.05$). However, when assessing the subtracted FDG-PET images in all of the AD patients additional areas of altered glucose uptake were identified.
Conclusion This is the first study to date which employs FDG-PET in conjunction with objective anosognosia assessment to identify the potential neural substrate of anosognosia in mild AD. Therefore, anosognosia may represent a specific defect in selective attention in AD.

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Patients with vascular dementia differ from patients with Alzheimer's disease with respect to population characteristics and pattern of cognitive decline

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Introduction Published data about the rate of cognitive decline and characteristics of patients with "pure" vascular dementia (VaD) have been limited. The objective of our study was to examine the population characteristics and pattern of cognitive decline in patients with VaD enrolled in randomised, double-blind, placebo-controlled, 24-week trials of the efficacy and tolerability of donepezil (Studies 307 and 308).
Method Enrolled patients had probable or possible VaD, classified according to NINDS-AIREN criteria. Patients were excluded if they had a diagnosis of Alzheimer's disease (AD).
Results 219 patients were enrolled; 73% had probable VaD and 27% had possible VaD. At screening, patients had a mean Hachinski score of 9.7. 73% of patients had had an abrupt onset of cognitive symptoms. 60% of patients had a history of at least one stroke, 17% had a history of transient ischemic attack. Vascular risk factors were prominent and included hypertension (70%), smoking (62%), and hypercholesterolemia (39%). Almost all patients had abnormal CT or MRI scans. Placebo-treated patients with VaD maintained cognitive function (ADAS-cog LS mean change from baseline score at Week 24 [observed cases], −0.10; n=310). This contrasts with the cognitive decline observed in placebo-treated patients with AD in donepezil trials (ADAS-cog LS mean change from baseline score at Week 24, 0.94; n=491).
Conclusion The patients enrolled in these trials had probable or possible VaD and a broad range of cardiovascular disease, and therefore differ from those enrolled in AD trials. Placebo-treated patients with VaD, in contrast to placebo-treated patients with AD, demonstrated stable cognitive function over 24 weeks.

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Global cognitive function and dementia in acute stroke and seven years after. The influence of age, stroke severity, stroke recurrence and stroke risk factors. A community-based study.

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Introduction Stroke may lead to impairment of global cognitive function and dementia. In a large community-based stroke cohort we evaluated risk factors for developing dementia following stroke.
Method In the community-based Copenhagen Stroke Study of 1197 acute stroke pts MMSE was tested in the acute state and at follow-up 7 years after. MMSE was used as a marker of dementia. Scandinavian Stroke Scale (SSS) was used to determine stroke severity. Relevant stroke risk factors were evaluated. Multivariate statistics were entertained.
Results Mean age was 74 years; at follow-up 81 years. MMSE was significantly related to stroke severity.
1) Acute state: SSS 0–14: MMSE 9; SSS 15–29: MMSE 12; SSS 30–44: MMSE 24; SSS 45–58: MMSE 24.
2) Follow-up: SSS 0–14: MMSE 9; SSS 15–29: MMSE 22; SSS 30–44: MMSE 24; SSS 45–58: MMSE 26.
Predictors of decline of MMSE over time were: *Age* MMSE decreased 0.7 point per 10 years increase (p=0.03). *Stroke se-*

verity MMSE decreased 1.0 point per 10 points decrease of SSS (p=0.02). *Hypertension* MMSE decreased 1.8 points (p=0.04). *Stroke* recurrence MMSE decreased 2.2 points (p=0.04). *MMSE in the acute state* MMSE decreased 6.6 points per 10 points decrease. Other stroke risk factors and leucoaraiosis had no influence.
Conclusion Change in MMSE over time was predicted by age, stroke severity, previous stroke, hypertension, and MMSE in the acute state. Atrial fibrillation, leucoaraiosis, and previous stroke had no independent influence. The study points to possibilities of preventing global cognitive impairment and dementia after stroke in particular hypertension.

SC 312

Intrathecal infusion test in the detection of normal pressure hydrocephalus

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Introduction We wanted to examine the frequency of pathological intrathecal infusion tests in the population of patients who were admitted to our department with a possible normal pressure hydrocephalus (NPH), and the proportion of patients who later had a shunt-operation.
Method All patients who had an intrathecal infusion test at the Department of Neurology, in the period 1991–2001 were included. The tests were performed according to the modified procedure of Katzman and Hussey. The initial resting pressure and mean increase in pressure during the 10 minutes of infusion were measured. The results from the tests were classified into 3 groups: normal, possible pathological and definite pathological.
Results During the 11 years 324 tests were performed. 168 tests were normal, 60 possible pathological and 96 definite pathological. In the group with pathological tests 16% of the patients were under 60 years of age, 23% 60–70 years, 47% 70–80 years, and 14% over 80 years of age. 56% of the patients with definite pathological tests, 20% with possible pathological tests and 14% with normal tests, later had a shunt-operation.
Conclusion NPH is a dementia that can be reversed with a shunt-operation. An early diagnosis is important. The intrathecal infusion test is a simple diagnostic procedure of significance. However, other factors also seem to influence in the decision regarding surgery.

Headache and pain

SC 313

Prevalence and diagnosis of migraine in a primary care setting

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Introduction This prospective, international, open-label study examined the association of headache impact and migraine diagnosis in subjects presenting to primary care physicians (PCP) with headache. Additionally, migraine prevalence in this primary care setting was ascertained.
Method Headache sufferers presenting to a PCP completed a headache impact test, a headache survey, and a productivity questionnaire. Then the PCP, using customary diagnostic practice, evaluated them, grouping them as being previously diagnosed migraine, newly diagnosed migraine, non-migraine primary headache, and secondary headaches. Newly diagnosed and non-migraine subjects completed diaries for their first 6 headaches. At study end, an expert panel reviewed the diaries, providing a final IHS diagnosis.
Results From 700 headache presenters (outside of US) who completed the screening phase, 82% (575/699) received a migraine diagnosis from their PCP; 170 were newly diagnosed subjects and 405 had been previously diagnosed. Non-migraine primary headache diagnosis comprised 92 subjects. Diaries were completed by 149 newly diagnosed migraineurs and 67 non-migraine subjects. Expert panel review of the diaries revealed that the initial migraine diagnosis in the newly diagnosed group was correct in 85% (126/148) of cases. Diary review of the non-migraineurs, as initially diagnosed by PCP's, revealed that 61% (41/67) could be reclassified as migraine (1.1/1.2).
Conclusion In the absence of headache diary information, PCP's appear to be too conservative in diagnosing migraine. When diagnosis (excluding migrainous) was made, it was correct 85% of the time. In contrast, 61% of non-migraine diagnosis by PCP's was in fact migraine (excluding migrainous).

SC 314

Headache associated with sexual activity: demography and clinical features

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Introduction The objective of our study was to provide demographical and clinical data about idiopathic headache associated with sexual activity (HSA) by analysing the second largest case series reported to date.
Method Between 1996 and 2001, 37 patients with a diagnosis of HSA were questioned by a structured interview.
Results The mean age at onset of the disease was 36.8 (±10.7) years. There were a clear male preponderance (2.7:1) and two peaks of age of onset. A first peak was between the 20th and 24th (n=8), a second between the 35th and 44th (n=16) year of age. 8 patients suffered from HSA type 1 (dull subtype) which gradually increased with progressing sexual excitement. The remaining (n=29) suffered from HSA type 2 (explosive subtype). The pain was predominantly bilateral (27/37) and diffuse or occipitally (33/37) located. In HSA type 2, there was a high co-morbidity with migraine (12/29), benign exertional headache (16/29), and tension-type headache (14/29). In contrast, HSA type 1 only had a co-morbidity with tension-type headache (4/8, $p<0.05$).
Conclusion Mean age at onset, a male preponderance, a predominantly bilateral and occipital pain, and a higher frequency of HSA type 2 are in concordance with the literature. For the first time, we found two peaks for the age of onset. The high co-morbidity of HSA type 2 with migraine and benign exertional headache might give interesting insights into its aetiology.

SC 315

Triptan use is not associated with increased risk of severe vascular events in migraine patients

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Introduction It has been speculated that triptan use might increase risk of ischemic events through vasoconstriction. Our main objective was to estimate rates of ischemic events in relation to triptan use among migraineurs and compared with non-migraineurs.
Method We conducted a retrospective cohort study of ischemic events and mortality among 130,411 migraineurs and 130,411 matched non-migraineurs, using United Healthcare's medical claims data from 1995–1999, and the National Death Index. Rate ratios (RRs) incorporate adjustment for demographics, cardiovascular history, ergot alkaloid use, and other factors.
Results Migraineurs and non-migraineurs had identical rates of myocardial infarction (MI): 1.4/1000 person-years. There was no increase in risk of MI with current (RR 0.80, 95% CI 0.58–1.11) or recent (RR 1.15, 95% CI 0.71–1.87) triptan use. Migraineurs had 67% more strokes than non-migraineurs (RR 1.67, 95% CI 1.31–2.13). Neither current (RR 0.90, 95% CI 0.64–1.26) nor recent (RR 0.84, 95% CI 0.46–1.55) triptan use was associated with risk of stroke. Current ergot use was associated with a moderate increase in risk of stroke (RR 1.49, 95% CI 0.93–2.41). History of migraine was not associated with all-cause mortality. There was no increase in all-cause mortality with current (RR 0.64, 95% CI 0.45–0.89) or recent (RR 1.01, 95% CI 0.63–1.64) triptan use.
Conclusion Use of triptans was not associated with increased risk of any ischemic events, including MI and stroke, or mortality. Consistent with previous studies, migraineurs had an elevated risk of stroke, compared with non-migraineurs. There is a suggestion for concern regarding ergot drugs and cerebral ischemic events.

SC 316

Reduced headache impact after three months of sumatriptan migraine therapy in the primary care setting

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Introduction The Headache Impact Test (HIT-6) was developed to quantify the impact of headache on patients' life. Sumatriptan has proven clinical efficacy; we aimed to evaluate its effect on reducing headache impact.
Method In a 15-country prospective study aimed to assess the association of HIT-6 scores with migraine diagnosis in the predominantly primary care setting (PCS), migraine subjects received sumatriptan 50mg (S50, n=595) for 3 months. At study end, changes in HIT-6 scores were evaluated for the overall study sample. To adjust S50 effect estimate for potential study effect using a conservative approach, the incremental change in HIT scores among subjects who were triptan naïves (TNs, n=457) over subjects who were prior sumatriptan users (PSUs, n=138) before the study was examined using analysis of covariance adjusting for gender and baseline score.
Results The study sample (n=595) consisted of 84% female, mean age 39 years. Prior to the study a majority of subjects (77%) did not use triptans, of which 83% used over-the-counter analgesics. At study end, mean HIT-6 score for the overall sample was significantly reduced from 65 (SD=6) to 59 (SD=8) ($p<0.0001$). After adjusting for potential study effect, reductions in HIT-6 scores during the study for TNs remains to be significantly greater than PSUs by 2.5 (95% CI: 1, 4) ($p<0.001$).
Conclusion Sumatriptan reduced headache impact beyond migraine pain and associated symptoms in triptan-naïve migraineurs.

SC 317

Topiramate prophylaxis in patients suffering from migraine with aura: results from a randomized, double-blind, placebo-controlled trial

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Introduction Topiramate, a broad-spectrum antiepileptic drug, has demonstrated efficacy in migraine prophylaxis in several pilot trials.
Method We conducted a multicenter, randomised, double-blind, placebo-controlled study of topiramate in migraine prophylaxis. A total of 213 patients were initially randomised in a 2:1 ratio to topiramate or placebo. Study medication was titrated weekly in 25-mg increments over 8 weeks to 200 mg/day or to the maximum tolerated dose, followed by a 12-week maintenance period. A subset of patients (n=75) experienced aura or migraine with aura (n=46 topiramate, n=29 placebo) at some point during the trial. The protocol defined analyses used ANCOVA with baseline monthly migraine rate as covariate.
Results For the ITT population (n=211), the protocol defined repeated measures were not sensitive enough to detect drug-placebo differences. Among patients with any aura, topiramate treated patients exhibited a significantly greater reduction in monthly migraine rate ($P=.018$) and migraine days/month ($P=.04$) compared to placebo treated patients.
Conclusion The results of this study suggest that migraine prophylaxis with topiramate may be more effective in patients with aura compared to those without aura.

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Efficacy of eletriptan in subjects who previously demonstrated lack of response to oral sumatriptan: a randomised, placebo-controlled study

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Introduction Eletriptan is a selective 5-$HT_{1B/1D}$ agonist previously shown to be effective in the acute treatment of migraine[1-3]. This study investigated the efficacy of eletriptan in a subset of patients from a previous study who discontinued sumatriptan due to lack of response.
Method A subgroup analysis was performed in a double-blind, parallel-group study of patients who previously had an insufficient response to sumatriptan (n=317). Subjects received

40mg eletriptan (E40; *n*=140), 80mg eletriptan (E80; *n*=121) or placebo (*n*=56) for the treatment of 1–3 migraine attacks.
Results Results are reported as E40, E80 and placebo. Two-hour headache response rates for eletriptan 40mg and 80mg were significantly greater than placebo (57%, 70%, 31%; $P<0.005$ E40, $P<0.0001$ E80). Both E40 and E80 provided rapid onset of action, with higher headache response at 1h (36%, 48%, 15%; $P<0.01$ E40, $P=0.0001$ E80). The 2h pain-free rate was significantly higher with eletriptan (30%, 46% and 4%; $P<0.005$ E40, $P=0.0001$ E80). Headache response was sustained, with no recurrence or need for rescue medication (37%, 45%, 13%; $P<0.005$ E40, $P<0.0005$ E80). Eletriptan demonstrated significantly superior sustained pain-free relief (21%, 28%, 4%; $P<0.05$ E40, $P<0.005$ E80). Treatment-related adverse events were generally mild to moderate and transient. Both eletriptan doses had significantly greater treatment acceptability than placebo (63%, 67%, 17%; $P<0.0001$ both comparisons).
Conclusion Eletriptan 40mg and 80mg were shown to be highly effective and well-tolerated in treating migraine patients who previously discontinued sumatriptan due to inadequate response.
Literature
1. Goadsby PJ *et al* (2000). *Neurology;* 54:156–163.
2. Stark R *et al* (2002). *Cephalalgia;* 22:23–32.
3. Diener H-C *et al* (2002). *Eur Neurol;* 47:99–107.

Movement disorders 2

SC 319

Brain activation during complex finger tapping in patients with writer's cramp: a functional MRI study.

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Introduction The objective of our study was to investigate the cerebral activation pattern during complex finger tapping in patients with writer's cramp.
Method We studied 11 patients with writer's cramp and 11 age-matched control subjects. All patients and controls were right-handed. Subjects had to tap individual fingers against the thumb pad in a fixed sequence (second-fourth-third-fifth) with the dominant and the non-dominant limb at their maximum speed. Right and left hand were studied in separate sessions. The fMRI experimental paradigm consisted of multiple 15-second epochs of baseline (rest) and activation (movement), in a boxcar configuration. Image processing and statistical analysis of the fMRI time-series data were performed using SPM99.
Results Both groups performed more taps with the dominant than the non-dominant hand. Patients performed a smaller number of finger taps than controls with both dystonic and non-dystonic hand ($F_{group}=145$; $F_{side}=21$; for both values $p<0.001$) and made more errors than controls ($F_{group}=11.4$; $p<0.01$). During movements of the dystonic hand patients activated bilateral premotor areas (BA6) and the left inferior parietal lobule (BA40) more than controls ($p<0.001$). In addition to these areas, during movements performed with the non-dystonic (and non dominant) hand patients also showed increased activation of the superior parietal (BA7) and insular cortex bilaterally.
Conclusion The performance of complex finger movements is abnormal in both hands in patients with writer's cramp. This abnormality is associated with an increased activation of the premotor and parietal cortex.

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Phenotypic characterization of dyt 13-related primary torsion dystonia in a large Italian family

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Introduction A large Italian family, affected by idiopathic torsion dystonia was investigated. The family was first examined in 1994. In 2001, a novel PTD locus named DYT13 was identified on chromosome 1(1p36.13–36.32), as associated with the phenotype segregating in this family.
Method The family, including 45 family members and 11 spouses, was examined for the first time in 1994. Each subject underwent complete neurological evaluation and was blood sampled for DNA analysis. All the members were re-evaluated on March 2000.
Results In 1994, 8 individuals received a diagnosis of definite dystonia and 6 of probable dystonia. After the second evaluation, 3 more individuals had developed a definite dystonia. Inheritance of PTD was autosomal dominant, with affected individuals spanning 3 consecutive generations and male-to-male transmission. The age at onset ranges from 5 to 45 years. Onset occurred either in the cranio-cervical region or in the upper limb. Progression was mild and disease course relatively benign for all affected individuals (just two cases had generalization). Affection of the lower body was rarely significant. No "anticipation" was observed in younger generations neither in the age of onset nor in severity. Some of the affected members presented rapid jerky, myoclonic-like movements.
Conclusion At present, the linkage of PTD and DYT13 locus has been detected only in this family. The phenotypic presentation of DYT13-PTD in 11 subjects belonging to a large Italian family is variable, but includes few prevalent features: early age at onset, upper body presentation of symptoms, mild severity of disease even in subjects with generalized dystonia.

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Role of levodopa on experimental pain in Parkinson's disease (PD): a positron emission tomography study

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Introduction Physiopathology of pain in PD is not well known. Painful symptoms could be in part due to central modification of nociception and that the dopaminergic deficit would be expected to eliminate the inhibitory influence on thalamocortical nociceptive activity. The objective of our study was to assess the effect of levodopa on cerebral activity during experimental nociceptive stimulation in PD patients and to compare pain threshold before and after administration of levodopa.
Method We performed $H_2{}^{15}O$ PET analyses of cerebral blood flow on six PD patients (66±8 years) while they received alternate noxious and innocuous right hand cold water stimuli during OFF dopaminergic treatment and after levodopa administration

(ON). Orders of cold stimuli and OFF/ON periods were randomised. For each patient cold stimuli were determinated using a visual analogue scale from 0 to 10. Noxious cold stimulus was defined as temperature inducing painful sensation superior or equal to 3 and innocuous stimulus was the previous value plus 10°C.
Results For most of the patients during OFF period, painful stimulation (9.3±1.2°C) induced increases of CBF in left parietal cortex, left motor and lateral premotor cortex, supplementary motor area, cingulum and brainstem. During ON period, only an increase of CBF in cingulate gyrus was elicited by pain stimulation (6.2±2.4°C). In OFF period, pain threshold was higher than in ON period (levodopa mean dose=225±61 mg) ($p=0.01$).
Conclusion Levodopa could reduced pain induced-activation in nociceptive pathways and raised pain threshold in PD patients suggesting that dopaminergic deficit could be involved in central processing of pain in PD.

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The adverse effects of L-dopa-induced dyskinesias on the quality of life (QoL) of patients with Parkinson's disease (PD): a prospective European study

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Introduction Previous studies have shown that dopamine agonists can reduce the risk of L-dopa induced dyskinesia. We evaluated the impact of L-dopa-induced dyskinesias on (QoL) in patients with Parkinson's disease.
Method A 6-month, multicentre, observational study was conducted in France, Germany and the United Kingdom. We measured dyskinesias using 2 scales: the Unified Parkinson's Disease Rating Scale (UPDRS, section IVa) and the Goetz Dyskinesia Rating Scale (GDRS). QoL was assessed using the Short-Form 36 (SF-36) and the Parkinson's Disease Quality of Life (PDQL) scales. Depression was evaluated using the Montgomery Asberg Depression Rating Scale (MADRS), and activities of daily living (ADL) using the UPDRS (section II). Statistical analysis included the use of multiple regression models to assess the impact of dyskinesias on QoL, while taking into account the effects of fluctuations, disease progression and country.
Results A total of 321 patients were enrolled at 63 centres: 63% of patients were male, mean age was 64 (±9) years, and mean disease duration was 8.7 (±5.6) years. There was a wide spectrum of clinical presentations ranging from no motor complications to fluctuations and severe dyskinesias. Higher dyskinesia scores on section IVa of the UPDRS were associated with a significant decrease in the QoL measures on the SF-36 subscales, as well as its two summary scales (physical component scale $p=0.0089$, mental component scale $p=0.0021$). Similarly, higher dyskinesia scores (UPDRS and GDRS) were associated with significant reductions in scores on the PDQL subscales; in particular, dyskinesias had a negative effect on the scores of the two subscales that were not symptom based (social functioning [$p=0.0002$ UPDRS; $p=0.0012$ GDRS] and emotional functioning [$p=0.0011$ and $p=0.0233$, respectively]). Dyskinesias also had an adverse effect on depression; higher scores on dyskinesia scales were associated with worsening depression on the MADRS ($p=0.0034$ for UPDRS and $p=0.0478$ for GDRS). On the other hand, dyskinesia scores had no significant effect on patients' ADL scores.
Conclusion L-dopa induced dyskinesias have adverse effects on the QoL of patients with Parkinson's disease. These effects are particularly important in terms of their negative impact on the psychological well-being of patients. Treatment strategies proven to reduce the risk of dyskinesia (use of dopamine agonists as early therapy) might help to diminish the adverse consequences of dyskinesias on the QoL of patients with Parkinson's disease.
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Hedonistic homeostatic dysregulation: screening in an Italian Parkinson's disease population

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Introduction Hedonistic homeostatic dysregulation (HHD) is a neuropsychiatric disorder that has recently been described in patients with Parkinson's disease (PD). The clinical syndrome of HHD includes symptoms of self-medication, drug hoarding, hypersexuality, behavioural disorders (aggression), mood disorders (depression, anxiety, hypomanic state) and an alterated perception of motor state.
Method To better evaluate the prevalence of this phenomena in PD, we have designed a short screening questionnaire that has been filled in at the control visits at our PD clinic. The questionnaire consisted of 3 parts: demographic data; presence of dyskinesias; 5 questions about 1- self-medication and assumption of extra dose of dopamine replacement therapy (DRT), 2- mood disorders, 3- behavioural disorders, 4- compulsive behaviours, 5- hypersexuality.
Results Over a 4-month period, 202 patients with PD have been screened; 114 were male, mean age was 68.1 y (range 42–89), mean duration of disease 7.3 y (1–30), mean Hoehn and Yahr score 2.2 (1–4). Of this cohort of PD patients, 43.6% (n=88) presented with mood disorders; 5.5% (n=11) abused DRT; 5.5% (n=11) showed behavioural disorders; 3,0% (n=6) compulsions; 2.0% (n=4) alterations of sexual behaviour. According to our data we have selected 6 (3.0%) patients who presented with abuse of DRT associated with mood and behavioural disorders, suggesting a possible diagnosis of HHD.
Conclusion HHD is a rare condition though extremely distressing for the patients, its family and social environment. We are evaluating in detail the selected patients to confirm diagnosis and consequently optimise pharmacological treatment.

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A biochemical marker for Parkinson's disease

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Introduction As the majority of neurodegeneration in PD occurs before motor dysfunction develops, the development of neuroprotective treatments for PD are hindered by current diagnostic methods based on motor signs. The death of central dopaminergic neurons results in the release of the intraneuronal pigment neuromelanin (NM). We hypothesised that the release of NM might stimulate a specific immune response and developed a novel enzyme-linked immunosorbant assay (ELISA) to quantify such a response. The aim of this project was to investigate

the efficacy of this test in discriminating PD subjects from healthy controls.
Method PD patients and healthy age- and sex-matched controls were recruited from Australian and German populations. PD was confirmed using the Unified Parkinson's Disease Rating Scale and a positive response to L-dopa in the absence of atypical signs. Collected sera were analysed using our novel ELISA test for anti-NM antibodies.
Results The ELISA response was significantly higher in the PD patients compared with healthy controls in both populations (Australian population; p=0.005, German population; p=0.001). The response was specific for catecholaminergic-based compounds and was unaffected by age or gender of the subject. The response was associated with disease severity, being higher in the early clinical stages.
Conclusion This test represents a novel and objective method to identify a specific immune response indicating the death of central dopaminergic neurons. As loss of pigmented neurons occurs primarily prior to the onset of motor symptomatology we propose that this test may represent a biochemical marker for preclinical PD.

Neuroimaging

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Positron emission tomography studies in patients referred with suspected Creutzfeldt-Jakob disease

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Method PET was performed in 15 patients with the tentative clinical diagnosis of Creutzfeldt-Jakob disease (CJD). [18F]-2-fluorodeoxyglucose (FDG) was used to assess changes in regional brain glucose metabolism indicative of neuronal death and the monoamine oxidase B inhibitor, N-[11C-methyl]-L-deuterodeprenyl (DED) was used to assess astrocytosis.
Results The diagnosis of definite CJD was confirmed in 6 patients. In 1 patient with probable CJD prion resistant protein could not be demonstrated. In further patients with probable CJD no autopsy was allowed. In the patients with definite or probable CJD, FDG and DED gave, in comparison with normal controls, a typical pattern of pronounced decrease of glucose metabolism regionally, indicative of cell death, accompanied by a similar increase in DED binding, indicating astrocytosis. These changes were most pronounced in the cerebellar, frontal, occipital and parietal cortex whereas the pons, the thalamus and the putamen were less affected and the temporal cortex appeared relatively unaffected. In the 6 other patients, the clinical examination was unable to confirm the diagnosis of CJD. In 3 of them a high regional cerebral glucose metabolic rate was noticed in parts of the brain, the temporal lobes and basal ganglia in particular. 1 had Sjögren's syndrome, 1 had suffered of paraneoplastic limbic encephalitis. The third spontaneously recovered. In the last 3 patients the deprenyl-binding was normal despite the hypometabolic glucose pattern similar to that seen in the CJD patients.
Conclusion A combination of a high regional deprenyl binding and a low regional glucose metabolism seems to be indicative of CJD.

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High resolution imaging of gene expression by positron emission tomography (PET)

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Introduction The objective of our study was to non-invasively quantitate herpes simplex virus type 1 thymidine kinase (HSV-1-tk) gene expression mediated by double-gene co-expression constructs by new generation ECAT HRRT and microPET scanners at high spatial resolution.
Method Multi-functional imaging genes consisting of the HSV-1-tk gene linked to the green fluorescent protein (gfp) gene by gene fusion or by an internal ribosome entry site were retrovirally transduced into rat F98 glioma cells. F98-TG17 (tkgfp fusion), F98-TIG (tkIRESgfp) and F98-GIT (gfpIREStk) glioma cells were sorted by fluorescence activated cell sorting (FACS) and their relative GFP-expression was quantified. The level of TK-expression was assessed after intravenous administration of 9-(4-[18F]fluoro-3-hydroxymethyl-butyl)guanin (FHBG; 250 μCi/rat; 50 μCi/mouse) into nude rats (n=4) and nude mice (n=4) bearing subcutaneous growing transduced F98 gliomas.
Results In cell culture, the relative level of GFP-expression mediated by F98-GIT cells was 2- to 3-fold higher than in F98-TIG cells indicating IRES-mediated impaired cap-independent translation of the second gene. In contrast, F98-TIG cells accumulated 2- to 3-fold more FHBG than F98-GIT cells demonstrating a good correlation between both quantitative assays for IRES-mediated GFP- and TK-expression in culture and in vivo.
Conclusion Subtle differences of HSV-1-TK expression due to different locations of the tk-gene within multiple-gene constructs can be differentiated by high-resolution FHBG-PET. Proportional IRES-mediated co-expression of TK with a therapeutic gene substituting the gfp-gene will enable indirect in vivo imaging of therapeutic gene expression even with the tk-gene located at the "weak" position downstream from the IRE site.

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Comparison of DW/PW-MRI and PET in acute ischemic stroke: early identification of penumbra and irreversible damage

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Introduction The main target of therapeutic strategies in acute stroke trials is the functionally impaired but still viable tissue, i.e. the penumbra. DW- and PW-MRI have become powerful tools in acute stroke trials. However, the quantitative assessment

of perfusional thresholds and irreversible lesion volume remain important methodological issues. MRI findings were validated on PET results to improve reliability in acute stroke imaging.
Method In 10 patients DW- and PW-MRI were performed within 8 h after ischemic stroke and after 24 h. MRI-based definition of hypoperfusion volume and lesion size was compared to CBF, CMR02, and flumazenil binding (FMZ).
Results The volume of reduced CMRO2 corresponded to DWI lesion size. Reduced FMZ binding could be larger than the DWI defect at first measurement and correlated to the permanent infarct. The area of critically reduced CBF extended beyond the defect on initial DWI and PWI but correlated to lesion size on DWI after 24h.
Conclusion These preliminary data in a small patient group allow the comparison of multitracer PET and DW/PW-MRI in the acute phase of ischemic stroke. PET imaging provides the earliest and most reliable detection of irreversible neuronal damage and penumbra tissue. However, in most instances MRI enables a fair estimate of ischemic compromise.

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Functional imaging of visually guided hand movements

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Introduction Imaging studies in humans suggest that visuomotor control of forelimb and eye movements involves reciprocal connections between striate, extrastriate, parietal, motor and frontal areas related to movement performance and visuospatial coding of movement direction. The aim of our study is to investigate the functional role of the human extrastriate visual area V5 in the control of visually guided hand movements and the interaction between extrastriate visual areas, basal ganglia, parietal and motor areas by using functional MRI (fMRI).
Method 9 right-handed, healthy subjects performed visually guided hand movements, either tracking a horizontally moving target or performing a centre out task to a stationary target by moving a cursor using a MRI compatible joystick. Subjects' eye and hand movements were monitored during scanning. Brainvoyager 4.4 was used for data analysis.
Results Our results show significant neural activations in area V5 during visually guided hand tracking movements. Visuomotor tracking with central fixation versus replay condition engaged a neural network involving left sensorimotor cortex, bilateral SMA, pre-SMA, dorsal premotor cortex, intraparietal cortex, as well as left basal ganglia, thalamus and right anterior cerebellum. The centre out task activated the same areas, but the basal ganglia and thalamus to a greater degree and less so the premotor cortex. Additional activation in the right red nucleus was evident.
Conclusion Our results indicate that visual monitoring during tracking and reaching requires the involvement of area V5.
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Functional brain mapping of the sensorimotor cortex: an fMRI study

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Introduction We wanted to implement a vibrotactile-stimulation-paradigm within the MR-environment for functional brain diagnosis in patients with severe motor deficits.
Method Experiments were performed on a 1.5Tesla whole-body scanner. The vibrotactile-stimulation-paradigm was a 50Hz vibrotactile stimulus with an amplitude of 2mm applied via pneumatic tube to the right and left palm. The vibrating device is an electromotor with 50W performance and 6000U/min. A single examination consisted of two fMRI measurements, where the right and the left palm were vibrated. The whole study was performed in 20 healthy, right-handed male and female volunteers (age range 25–45 years). Statistical analysis was done with SPM99.
Results Vibratory stimulation of the right and left palm revealed contralateral activation of the primary motor cortex (MI), the primary and secondary somatosensory cortex (SI and SII) and the premotor area (PM). The supplementary motor area (SMA) within the frontal lobe was bilaterally activated. An ipsilateral activation foci was seen within the gyrus frontalis superior near the interhemispheric fissure, within the PM and the SI and SII. The strongest activation was found within the SI and SII followed by the MI. The PM and the SMA showed only weak activation.
Conclusion Vibratory stimulation to the right and left palm can lead to an activation response not only of sensory cortex, but also to an activation response of the motor cortex. This holds promise for the vibratory stimulation to be applied for functional brain mapping of the sensory motor cortex in patients with severe motor deficits.

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Investigations on the human central sympathetic pathway through the brainstem using a new method of three-dimensional mapping on the basis of digital post-processing MRI

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Introduction Information on the brainstem segment of the central sympathetic pathway is sparse. Experimental studies suggest integrative centres in the dorsolateral pontine tegmentum and in the medulla oblongata. To study the central sympathetic pathway in man we applied a new method of three-dimensional brainstem mapping using digital post-processing MRI by

superimposing brainstem lesions onto the appropriate sections of an anatomical atlas and an idealized brainstem model.
Method 258 prospectively recruited patients presenting with acute signs of brainstem ischemia underwent biplane T2- and EPI-diffusion weighted MRI with slice direction parallel and perpendicular to a brainstem slice selection of the stereotactic anatomical atlas of Schaltenbrand and Wahren. The individual slices were normalized and projected into the digitalized anatomical atlas. Lesions were then imported into a three-dimensional model of the human brainstem consisting of 5286 volume elements ("voxels") for correlation analysis.
Results 32 of the 258 patients showed a Horner's syndrome due to acute brainstem ischemia. Only 2/32 patients had pontine lesions sparing the medulla, 14 had pontomedullary lesions, 16 medullary lesions. Correlation analysis showed significantly affected voxels in the dorsal medulla oblongata. Lesion site contacted or overlapped the area of the dorsomedially located Nucleus tractus solitarius (NTS) in 82% of the patients on one or more atlas slice levels.
Conclusion In this first in vivo study important relay centres of the central sympathetic pathway could be localised in the medullary complex of the NTS, one of the integrative centres suspected from experimental animal studies.

Sleep disorders

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Sleep apnoea in ischaemic stroke: a prospective study

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Introduction Sleep apnoea can be responsible for various changes that can play an important role in precipitating stroke. We aimed to prospectively evaluate the presence of sleep apnoea syndrome (SAS), delineate its subtype, and evaluate its management in recent stroke.
Methods We investigated 50 patients with acute stroke and 27 subjects as a control. We obtained data reflecting risk factors and Epworth Sleeping Scale (ESS) by interviewing every subject and his/her spouse. Severity of stroke was assessed by Scandinavian Stroke Sclae (SSS). Patients and control were subjected to overnight sleep study using portable AutoSet device. Arterial blood gases were estimated for very patient and control.
Results 30 patients had supratentorial and 20 had infratentorial infarctions. Among the supratentorial group, 7 (23.3%) had obstructive SAS, while in infratentorial group 6 (30%) had central and 5 (25%) had obstructive SAS. No significant difference was found between obstructive SAS, central SAS, and control groups as regards age, BMI, other risk factors, while ESS was significantly higher in obstructive than in central and control groups. Sleep respiratory study parameters were significantly higher among obstructive than central SAS and control groups. No relationships were found between sleep apnoea and the topographical parenchymatous location of the neurological lesion. On the other hand, significant correlation was found between severity of stroke and severity of SA. All patients with obstructive SAS showed significant improvement after nasal continues positive air pressure (CPAP) ventilation, and those with central SAS improved significantly with bilevel positive airway pressure (BiPAP).

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Hypocretin dysfunction and sleep disturbances in neurological diseases

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Introduction Hypocretins 1 and 2 are newly discovered neuropeptides that play an important role in the regulation of sleep. Recent human studies documented a high sensitivity and specificity of undetectably low CSF hypocretin levels in idiopathic narcolepsy-cataplexy cases.
Method 20 patients with narcolepsy-cataplexy, 4 cases with Niemann-Pick disease and 3 patients suffering from Prader-Willi syndrome underwent sleep study (nocturnal v-PSG and MSLT). In all of the patients HLA oligotyping with DQB1*0602 positivity was done, hypocretin-1 measurement in CSF was provided and the values were correlated with controls.
Results MSLT mean value in patients suffering from narcolepsy-cataplexy was 3.06±2.3 min, number of SOREMs/5 was 2.5±1.57. With the exception of 2 cases (one of the both with signal peptide hypocretin mutation) the others were HLA DQB1*0602 positive. 17 out of 20 patients had undetectable CSF hypocretin-1 level, in one case the level was very low (75 pg/ml). Only 1 patient showed normal and 1 even elevated CSF hypocretin-1 level. The diagnostic specificity of this examination for narcolepsy was 90%. Out of 4 Niemann-Pick disease cases only one with clinical signs of cataplexy was HLA DQB1*0602 positive. CSF hypocretin-1 level in this group was significantly diminished ($p<0.05$) in comparison with the controls. Patients suffering from Prader-Willi syndrome (n=3) revealed a diminished CSF hypocretin-1 level in correlation with duration of the disease and severity of sleep disturbance.
Conclusion Hypocretin deficiency can be found besides narcolepsy-cataplexy also in sleep disorders developing as a consequence of lateral hypothalamic area damage.

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Effects of gabapentin on restless legs syndrome accompanied by nocturnal pain: results of a double-blind, crossover study with polysomnographic control in 24 patients

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Introduction Several open studies have suggested the therapeutic efficacy of gabapentin (GBP) in restless legs syndrome (RLS)[1,2]. This double-blind study investigated efficacy and effective dose of GBP in RLS and examined the role of nocturnal pain in predicting GBP response.
Method 24 patients with RLS (International Restless Legs Syndrome Study Group [IRLSSG] criteria)[3] underwent 6 weeks of treatment with GBP or placebo (PLB) following a randomised, double-blind, crossover design. GBP was initiated at 600mg/d and increased by 600mg/d every 2 weeks if clinically required. Patients were assessed at baseline with a visual analog scale for pain (VAS-P) and the IRLSSG rating scale. Based on a threshold score of 20mm on the VAS-P, patients were classi-

fied as either pain-RLS (P-RLS) or not pain-RLS (NP-RLS). Both rating scales were completed every 2 weeks. Sleep studies were performed after each treatment period.
Results The mean IRLSSG-rating score for GBP patients was 53% lower than for PLB patients. The mean effective dose of GBP was 1855mg/d. GBP also increased total sleep time, sleep efficiency, and stage 3 sleep, and reduced periodic leg movements of sleep (PLMS) (all $p<.05$). Additionally, the percentage of NP-RLS increased with GBP (62% to 81%) but remained stable with PLB ($p<.01$).
Conclusion GBP is an effective treatment for RLS. The presence of nocturnal pain predicts a better response to GBP. Normalization of sleep and PLMS-index can be observed following GBP treatment.
Literature
1. CH (1997). *Clin Neuropharmacol*; 20:148–151.
2. Happe S et al (2001). *Neurology*; 57:1717–1719.
3. Walters AS (1995). *Mov Disord.*; 10:634–642.

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The impact of restless legs syndrome (RLS) on sleep and cognitive functioning

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Introduction RLS is a serious neurological disorder with primary morbidities involving sleep loss and extreme discomfort, which may impact on cognitive abilities. To date, no studies have systematically assessed the burden of RLS on sleep and cognition. This study assesses the impact on these parameters compared with a normative population (norms).
Method The Medical Outcomes Study Sleep and Cognition scales were administered to 85 patients with primary RLS referred to a specialist clinic. Scores from this group were compared with published norms (N=3053). As recommended in the literature, a 0.5 SD determined a minimally clinically important difference.
Results The majority (64.5%) of patients were women; the mean (±SD) age was 62.4 (±14.0) years; 67.1% reported experiencing RLS symptoms almost daily. Sleep scores for the RLS group were 19 points (approximately 1 SD) worse than the norms. Cognition scores for the RLS group were 14 points (0.5 SD) worse than the norms. Sleep and cognition scores for RLS patients were even worse if RLS symptoms first began to appear before the age of 45 years (deficit of four additional points). A significant correlation between sleep loss and cognition was noted ($p<0.05$).
Conclusion RLS poses a clinically significant burden to patients in terms of sleep loss and cognitive functioning, which should be considered when evaluating RLS treatment. The early-onset phenotype was more impaired. This is consistent with research noting the biological differences between early- and late-onset RLS phenotypes. Future studies will further establish the cognitive and sleep impact of RLS.

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Cabergoline in restless legs syndrome (RLS) – a double-blind placebo-controlled multicenter dose-finding trial

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Introduction Augmentation or time-shifting of symptoms after starting therapy may limit the clinical use of l-dopa (LD) and short-acting dopamine agonists (DA) in RLS. Trials suggest an inverse correlation between half-life and incidence of augmentation, favouring DAs with longer half-lifes, like cabergoline (CAB, t1/2: 65h).
Method 86 patients with moderate to severe RLS were stratified into 4 treatment groups receiving placebo, 0.5mg, 1mg and 2mg CAB once daily.
Results Demographic characteristics were comparable in all groups: duration of RLS: 220.4±158.2 months, previous LD/DA use: 60.7/44%, RLS severity at night: 6.5±1.9. Between baseline and week 5 all three CAB treatment groups showed a clinical improvement of 1) RLS severity at night (0.5mg: 6.7±1.8 vs. 2.3±2.8, p=0.0046; 1mg: 6.0±1.3 vs. 1.9±2.5, p=0.0085; 2mg: 7.0±2.3 vs. 2.2±3.2, p=0.0016), in contrast to placebo (6.2±2.0 vs. 4.8±3.2). Similar results have been found for the RLS severity before bedtime (0.5mg: p=0.0426; 1mg: p=0.0041; 2mg: p=0.0137), 3) RLS severity at day (0.5mg: p=0.3512; 1mg: p=0.0126; 2mg: p=0.0021), 4) IRLSSG rating scale (0.5mg: p=0.0013; 1mg: p=0.0017; 2mg: p=0.0032) and 5) satisfaction with sleep (0.5mg: p=0.0449; 1mg: p=0.0561; 2mg: p=0.0038). AEs with possible relationship to any study drug were comparable among groups; no serious AE occurred.
Conclusion Cabergoline is a highly efficacious and well tolerated option for the treatment of RLS patients. While even low doses of 0.5mg CAB given once daily in the evening led to a significant improvement of RLS symptoms at night, a single evening dose of 2mg covers RLS symptoms over the whole 24h period.

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Transient restless legs syndrome (RLS) can be induced by spinal anaesthesia – a prospective study.

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Introduction Restless Legs Syndrome (RLS) is a frequent neurological disorder with prevalence about 10%. The following study is based on several patients describing RLS after undergoing surgery in spinal anaesthesia. The aim of this study was to examine the possible relationship between RLS and spinal anaesthesia in a prospective way, to assess the incidence and time course of RLS after spinal anaesthesia and to identify possible predictors.
Method We examined 202 consecutive patients undergoing spinal anaesthesia for various surgical reasons. We regarded prospectively the presence and severity of RLS symptoms with Irlssg criteria and severity scale 48–72 h post surgery, after one week, one month, 3 and 6 months. At the first contact a detailed medical history including prior RLS symptoms and current drug treatment was obtained. Additionally, blood biochemical parameters and the total blood count were taken from the patients' histories.
Results 161 of the patients had no prior history of RLS symptoms. From this group 14 patients (8.7%; 95% CI 5.0–13.3) developed first onset RLS after spinal anaesthesia. The RLS symptoms were transient with a mean duration of 33±30 days. Regarding the group of patients with pre-existing RLS (n=41) 4 of them developed a marked deterioration of RLS symptoms. Low MCV and MCH were identified as predictors of RLS symptoms after spinal anaesthesia ($p<0.02$).
Conclusion Transient RLS can be caused by spinal anaesthesia.

Cognitive neurology

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Neuropsychological impairments acute and seven years after stroke The Copenhagen Stroke Study

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Introduction Neuropsychological impairments are significant contributors to the handicap of the stroke patient. We wanted to study their presence late after stroke in a 7-year follow-up study.
Method In the community-based Copenhagen Stroke Study of 1197 acute stroke patients neuropsychological impairments (aphasia, apraxia, hemineglect, anosognosia, orientation and global cognitive function (MMSE ≤24)) were tested on admission and at follow-up 7 years later. Stroke severity was measured on admission and at follow-up using the Scandinavian Stroke Scale (SSS, 0–58).
Results 1197 patients were included (mean age 74 sd 5 years). 324 pts (27%) were alive at follow-up (84 sd 8 months). 166 (53%) accepted to participate. 24 had suffered a new stroke. In total 142 pts were included in the study (mean age at stroke onset 66 sd 14 years). Participants had less severe strokes on admission (SSS 47><SSS 44 years, p=.03). No significant age difference between participants (66 sd 14 years) and non-participants (68 years sd 18 years). No significant difference in frequencies of neuropsychological impairments on admission.
Frequencies of neuropsychological impairments acute and after 7 years were: Aphasia 38%/21%; orientation 23%/14%; apraxia 7%/6%; hemineglect 16%/12%; anosognosia 16%/12%; MMSE ≤24 42%/25%. In 53% a specific impairment or MMSE ≤24 was present.
Conclusion The frequency of neuropsychological impairments late after stroke is surprisingly high and contributes to the handicap in more than half of the long-term survivors.

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Illusory contours and specific regions of human extrastriate cortex: evidence from rTMS.

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Introduction fMRI studies showed that perception of illusory contours is associated with extrastriate cortex activation prevailing on the right side. 1 Hz rTMS is able to induce lasting inhibition of cortical activity. The objective of the study was to investigate the role of extrastriate cortex in illusory contour perception inducing 1 Hz rTMS interference in healthy subjects.
Method We studied 8 healthy subjects (4 M, 4 F; mean age: 41±10.5; range 25–55 yr). 1 Hz rTMS (600 pulses) was given through a figure-of-eight coil over right and left occipital cortex (O1 and O2 of 10/20 EEG system) at 90% motor threshold intensity. To control for unspecific rTMS effects, sham magnetic stimulation on the same sites was given. Subjects underwent computerized task requiring perception of illusory and real contours of Kaniztsa squares in baseline and after rTMS. After stimulus presentation the subject made a forced-choice decision about the regularity or irregularity of stimulus contours by hitting, as soon as possible, one of two keys on a keyboard. Reaction times (RT) were measured.
Results Right occipital stimulation significantly increased RT for illusory contour perception (p<.0001 vs. all other experimental conditions at Duncan's post-hoc). On the other hand, no significant RT changes were observed in the other experimental conditions with respect to the baseline.
Conclusion 1Hz rTMS of right extrastriate cortex can disrupt perception of illusory contours and the effect appears to be side-specific, being evident only after O2 stimulation. This rTMS study supports the critical role of right extrastriate cortex in intermediate vision.

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Alteration of effector versus side of movement: a contingent negative variation (CNV) study

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Introduction Earlier research has explored the impact of several stimulus- and set-related parameters on brain activation as measured by the amplitude of the Contingent Negative Variation (CNV). Little is known, however, about the impact of the previous trial on the CNV of the forthcoming trial and how a previous movement affects brain activation preparing the next movement. Our study was designed to examine such effects of alteration of finger (from index to middle, and vice versa) and hand (from left to right, and vice versa) independently from each other.
Method CNV was recorded in 20 right-handed healthy subjects using a visual/visual S1-choice paradigm. An earlier informative stimulus instructed for side and finger of the following movement and was followed 3s later by an imperative stimulus providing the command to move. Subjects had to respond to each imperative stimulus with a unilateral flexion movement made with index or middle finger of one hand. Every finger of a previous trial could be followed by the same or every other finger in the next trial with equal probability. CNV was analysed with respect to finger and hand of the present and the preceding movement.
Results Our results show that: (1) a change of the side of movement is associated with a widespread increase of negativity contralateral to the currently prepared movement. (2) After a change of finger, a more focal increase of negativity occurs over temporoparietal areas contralateral to the currently prepared movement. (3) A change of finger results in higher negativity over the left hemisphere.

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The prevalence of Fahr's disease among patients presenting with Parkinson-like syndrome and mild cognitive impairment

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Introduction Absence of response to Levodopa is considered as one of the most important factors to reconsider a diagnosis of Parkinson Disease (PD). Fahr's disease (idiopathic basal ganglia calcification) is a rarely reported condition among the abovementioned cases. The objective of our study was o identify the most common causes of Mild Cognitive Impairment with extrapyramidal signs not responding to Levodopa treatment
Method We retrospectively reviewed the personal files of 138 patients with clinically definite PD with dementia (Calne et al, 1992), treated for a period of 1 year with L-Dopa as the main

therapy. All patients were re-examined at 6 and at 12 months after presentation in our outpatient clinic. We performed regular evaluations with the UPDRS. Patients not responding to Levodopa treatment have undergone a full investigation, including neuroimaging studies and a neuropsychological evaluation (MMSE, SKT tests and ADAS cog).
Results Of the 138 patients, 27 were identified as non-responders to Levodopa after 1-year treatment. From these patients, 11 were identified as probable Alzheimer Disease (AD) (NINCDS-ADRDA criteria), 7 as probable Lewy Body Disease (LBD) (McKeath and al, 1996), 2 as Multiple System Atrophy, 5 as Fahr's Disease and 1 as pseudodementia.
Conclusion Fahr's disease is a rare, yet underdiagnosed, cause of Parkinson-Like Syndrome non-responding to Levodopa. Taking into account the facility of the diagnosis with neuroimaging studies, as well as the familial-hereditary character, we propose that detailed neuroimaging studies (especially a CT-scan) in association with neuropsychological investigation should be performed in all of those patients, and possibly in their relatives as well.

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Evaluation of executive functions in Parkinson's disease by conditioned choice reaction time testing

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Introduction Parkinson's disease (PD) causes cognitive changes that may occur early (Cooper et al, 1991; 1994) or even precede motor symptoms. These changes involve mainly frontal executive functions. We tested the validity of a new computer based conditioned choice reaction time test (CCRTT) for quantitative evaluation of executive functions in PD. The CCRTT demands establishment of arbitrary associations between visual and auditory signals, quick changes of these associations and refrainment from automatic responses. This new test is objective, quantitative, independent of linguistic skills, simple to administer and culture-independent.
Method 19 early PD patients and 21 age-matched controls were tested. The patients had significantly slowed visual and auditory choice reaction times.
Results When tested on learnt associations between visual cues and auditory stimuli, patients were as fast as controls. In the final test condition the learned visual-auditory associations were reversed unexpectedly in 25% of the trials. Both patients and controls became slower in the regular trials and were further slowed in the reversed trials (patients: $p=0.001$, controls: $p=0.00004$). Marked differences between the two groups were found in the regular ($p=0.002$) and reversed ($p=0.003$) trials.
Conclusion The results show that PD patients are able to use learnt associations in order to shorten their auditory reaction time down to normal. However, they required extra time to switch their planned response in the reversed condition. This is consistent with their perseverance, as demonstrated by computer-administered WCST. We conclude that this new CCRTT is a sensitive and valid test for executive capabilities.

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Attention and short-term memory in patients with mild to moderate traumatic brain injuries

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Introduction Mild to moderate traumatic brain injuries (TBI) represent 75% of head injuries. Long-lasting symptoms are reported in 14 to 88% of such patients. Since imaging techniques, EEG, and neurological examination reveal no signs of cerebral damage, there are controversies about the existence of cognitive deficits in such patients.
Method We developed computerised tests for visual attention and short-term memory assessment. We compared the results of 37 patients with TBI and 57 controls.
Results Our results show that the registration of correct answers is not sensitive enough to discover cognitive deficits in TBI patients, but significant difference is found in results of recognition reaction time ($p<0,05$) measured with Sternberg Memory Scanning Paradigm and time of reaction to visual stimulus ($p=0,0348$) measured with Choice Reaction Time Task.
Conclusion We showed that it is possible to measure the reduced efficiency of TBI patients in performing the same task as controls. This can be and objective measure of mental slowness that TBI patients often report.