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Abstracts
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Freie Mitteilungen SNG

Are dual-task related gait changes influenced by frontal lobe dysfunction in demented older adults?

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Background: Frontal lobe dysfunctions (FLD) contribute to gait changes in the elderly but the precise mechanisms are still poorly understood. Dual-task related gait changes (DTRGC) depend in part on the capacity to appropriately allocate attention between tasks performed simultaneously and are mainly related to executive deficits. Therefore, a good understanding of DTRGC in demented subjects with FLD of variable severity could help to clarify the role of the frontal lobe in motor gait control.

Objective: To quantify and compare mean values (MV) and coefficients of variation (CV) of stride time under single- and dual-task condition in demented older adults with and without FLD as well as in non-demented older adults.

Methods: Stride time parameters were collected using a GAITRite®-System in 56 older adults (22 without dementia; 16 demented without FLD and 18 demented with FLD) at self-selected speed while (1) walking alone and (2) walking with backward counting. Demented older adults were separated into 2 groups according to the Frontal Assessment Battery (FAB).

Results: MV of stride time while walking alone was higher in demented subjects with FLD compared with those without FLD ($p < 0.05$) and non-demented subjects ($p < 0.05$). Compared to walking alone, the MV of stride time increased significantly while backward counting in demented subjects ($p < 0.05$), whereas a decrease ($p < 0.05$) was found in non-demented subjects. CV of stride time was solely higher in subjects with FLD compared to non-demented subjects ($p < 0.05$) in both walking conditions. Simple linear regression showed a significant association between a low score at FAB and a high stride time variability while walking alone ($p = 0.005$).

Conclusion: Those findings confirm the contribution of FLD in DTRGC and suggest that stride time could be a quantitative marker to distinguish among normal subjects, demented patients with and without FLD.

Association of regional grey-matter volume loss and progressive white-matter lesions in multiple sclerosis

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Background: Previous studies have established regional grey-matter (GM) volume loss in multiple sclerosis (MS) but the association between development of white-matter (WM) lesions and changes of regional GM volumes is unclear.

Objectives: The aim of the present study was to clarify this issue by the use of VBM, a non-biased measure of regional differences in GM volumes. We predicted that regional GM volume reductions predominantly occur in patients with increasing WM lesion volumes. Additionally, we hypothesised that a core group of patients with both increasing T_1- and T_2-lesion burden would show volumetric GM reductions that are qualitatively similar but more pronounced than in patients with T_2-lesion progression alone.

Methods: T_1-weighted three-dimensional MRI data from 212 MS patients followed up for 12 months were analysed using VBM. An analysis of covariance (ANCOVA) model assessed with cluster-size inference (all corrected $p < 0.05$) was used to compare GM volumes between baseline and follow-up while controlling for age, gender and disease duration. Volumes of T_1-hypointense and T_2-hyperintense lesions and the number of new T_2 lesions were determined.

Results: Comparing all MS patients ($n = 212$) longitudinally, GM volume remained unchanged during one-year follow-up (corrected $P = 0.544$). In patients with relapsing remitting MS (RRMS) and increasing T_2-lesion burden ($n = 67$) significant cortical GM volume loss occurred in the fronto-temporal cortex (e.g. anterior cingulate gyrus and cerebellum). In RRMS with increasing T_2-predominantly and T_1-lesion burden ($n = 45$) additional clusters occurred in the insula bilaterally as well as in frontal areas. In contrast, patients lacking an increase in white-matter lesion burden over time did not show GM changes.

Conclusions: Overall, the progression of regional GM volume reductions seems to require white-matter lesion progression and predominantly occurs in cortical areas related to cognition.

Facets of sleepiness in patients with hypersomnolent depression in comparison to narcoleptic and obstructive sleep apnoea patients

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Background: Excessive daytime sleepiness (EDS) is the major subjective complaint of patients with various sleep disorders including sleep insufficiency syndrome, inadequate sleep hygiene, obstructive sleep apnoea syndrome (OSAS), periodic leg movement disorder (PLMD), narcolepsy and idiopathic hypersomnia. Patients with major depression typically report on daytime fatigue, lack of energy and possibly also insomnia but not EDS. However, a subgroup of depressed patients suffers from hypersomnia, which is a characteristic symptom in atypical or seasonal affective disorder. This group with "hypersomnolent depression" (HD) is occasionally difficult to differentiate from monosymptomatic narcolepsy or idiopathic hypersomnia on clinical basis alone.

A pilot study was undertaken in order to define whether vigilance testing could help to differentiate between these entities.

Method: Polysomnography, the Epworth sleepiness scale (ESS), multiple sleep latency test (MSLT), Steer Clear test and pupillography were retrospectively compared between 19 patients with HD, 23 patients with narcolepsy and 46 patients with mild obstructive sleep apnoea syndrome (OSAS).

Results: The percentage of female patients was 63% in the depression group, 47% in the narcoleptics and 9% in the OSAS group. The OSAS group showed a significantly higher age ($p < 0.001$) that was used as a covariate in the statistical analysis of the variables. The ESS score confirmed a moderate to severe subjective EDS in all patient groups, as requested in the inclusion criteria, without statistical differences between groups. The mean sleep latency of the MSLT was significantly shorter in the narcoleptic group (2.5 min) as compared to both other groups, underlining the greater sleep propensity in narcolepsy. There was no difference of sleep latency between OSAS (7.2 min) and HD (8.1 min). The borderline mean sleep latency of 8.1 minutes (normal >10 min) in the group with HD objectively confirms a mild EDS in these patients. The error rate in the Steer Clear reaction time test was non-significantly greater in depression than in narcoleptics (10.4 and 7.9%; n.s.) but significantly greater than in OSAS patients (10.4 vs 5.9%; $p < 0.01$). A similar trend was found for the pupillary unrest index (PUI) which was greatest in narcoleptics (11.5), with similar values in depression (9.2) and in OSAS (7.4) (n.s.).

Discussion: ESS in patients with HD could be confirmed by the MSLT. Moreover we found an unexpected high error rate in the Steer Clear reaction time test in depressed patients, statistically not different from the result in narcolepsy. In the view of the milder sleepiness in HD patients as assessed by the MSLT, we hypothesise that the higher error rate in this active reaction time test in HD is based on neuropsychological factors unrelated to EDS such as reduced motivation and attention. Conversely, we conclude that a high error rate in the Steer Clear reaction time test in subjectively sleepy (ESS) but objectively (MSLT) not or only slightly sleepy patients is suggestive of non-organic hypersomnia.

Is conventional MRI insufficient to reflect residual disease activity in multiple sclerosis patients treated with Natalizumab?

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Natalizumab (Tysabri®) is the first ∝4-integrin antagonist in a new class of selective adhesion-molecule inhibitors used for the treatment of multiple sclerosis. Natalizumab was approved for the treatment of adults with highly active relapsing-remitting multiple sclerosis in the European Union in June 2006 and in Switzerland in July 2007.

At the University Hospital Zurich, the first treatment with Natalizumab was started in November 2006. Until July 2008 Natalizumab treatment has been initiated in 50 patients suffering from severe multiple sclerosis. 18 patients have been treated for more than one year. Complete medical examination using the Expanded Disability Status Scale (EDSS) was done before treatment initiation, at month 6, 12, 18, etc., and when a patient complained of new neurological symptoms. MRI scans of the brain were performed shortly before treatment and after 12 months, or in the case of a severe relapse.

16 patients experienced relapses during Natalizumab treatment, 2 of these patients had two relapses during the first year, 2 patients had a relapse in the first and second year respectively. 4 patients had severe relapses during their first or second Natalizumab treatment cycles. In spite of high-dose corticosteroid treatment, relapses lead to persisting neurological impairment in 5 patients. In contrast, 6 patients had an improved EDSS after 12 months of treatment. 5 patients discontinued treatment, 3 because of ongoing disease activity, 2 patients because of unrelated psychological problems.

The cranial MRI scans performed before start of Tysabri® treatment showed active lesions with Gadolinium enhancement in 20 patients. In the other patients inflammatory disease activity was demonstrated by new T_2 lesions. In the follow-up MRI scans after one year no new or Gd-enhancing lesions could be seen in any of the patients, including those who had suffered relapses. To our surprise, even in MRI scans performed during a clinical relapse no inflammation was detectable.

Natalizumab treatment stabilised clinical disease activity in the majority of our patients and suppressed the formation of new MRI lesions. Even in patients still experiencing clinical relapses MRI scans did not indicate inflammatory activity. This raises the question whether (a) relapses under Tysabri® treatment are caused by different, "noninflammatory" mechanisms or (b) conventional MR imaging is insufficient to monitor disease activity under Tysabri® treatment.

Lateralisation of dynorphin gene expression in the rat striatum

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Cortical lateralisation of brain function is well known in humans. However, lateralisation in subcortical structures, like basal ganglia, is much less understood. In particular, it is unclear if the striatum presents a lateralisation of function or not, even though previous studies have suggested an asymmetry in dopaminergic nigrostriatal pathways. Our hypothesis is that striatal direct and indirect pathways are differentially expressed in right and left striatum.

We analysed, in healthy rats, the striatal expression of dynorphin (DYN) and enkephalin (ENK) mRNA, as markers of the direct and indirect pathways respectively, and glutamic acid decarboxylase (GAD) mRNA expression, as a marker of global GABAergic activity. The striatum was divided into two sectors medial and lateral and we compared the expression of the different markers in right and left striatum.

DYN and GAD mRNA expression was higher on the left hemisphere in the medial sector of the striatum, but not in the lateral one. We did not observe any difference between both sides with ENK mRNA expression.

In conclusion, our data suggest a predominance of the direct pathway on the left side. This effect could be rather related to limbic function than to motor function, as it is specific to the medial part of the striatum. This finding may be important to understand symptoms induced by disease affecting the basal ganglia in an asymmetric fashion like Parkinson's disease.

Post-stroke seizures and epilepsy

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Background: Stroke is the leading cause of epilepsy after the age of 60. The published incidence of post-stroke seizures and epilepsy varies from 4.4 to 42.8% according to different study designs.

Methods: Our semi-prospective study included 599 first-ever stroke cases admitted to our hospital between January 2002 and December 2004. Patients with a prior history of stroke, epilepsy, haemorrhagic stroke or other possible causes of epilepsy (e.g. brain tumour, alcohol dependence) were excluded

from the study. The follow-up period to identify stroke-related seizures was of a minimum of 36 months, in average 49.5 months. Post-stroke epilepsy was related to clinical factors (age, sex, onset stroke severity, lesion size, localisation, stroke subtype and stroke-risk factor profile) and divided into "early onset" and "late onset" seizures occurring either within 7 days or more than one week after stroke, respectively.

Results: Of all patients, 5.18% developed seizures after stroke, of whom 2.18% experienced a single epileptic seizure and 3.0% developed epilepsy with recurrent seizures. Early-onset seizures were detected in 25.8% and late-onset seizures in 74.2%. Predictors for developing vascular epilepsy are severity of initial neurological impairment, large lesions with cortical involvement and anterior circulation syndrome. No significant differences were observed in clinical predictors between early- and late-onset seizures, neither in single seizure nor in epilepsy. But a larger number of patients with late-onset seizures developed epilepsy.

Conclusion: We found a rather low incidence of 5.18% of post-stroke seizures, which may be due to our strict exclusion criteria for potential epileptogenic pre-morbidities. In other studies this may be overestimated. As others, we also found more severe neurological impairment, large lesions with cortical involvement and anterior circulation syndrome to be predictive factors for post-stroke seizures.

Status epilepticus in a tertiary care centre – epidemiological and clinical characteristics and a dichotomised treatment and outcome analysis

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Rationale: Epidemiology and clinical characteristics of status epilepticus (SE) in a single tertiary care centre may differ from those in population-based studies.

Methods: Retrospective 3-year analysis of epidemiological and clinical data of a cohort of patients with SE in a tertiary care centre. The observation period included the time from onset of SE until hospital discharge. Parameters assessed were sex, age, SE duration, SE type, treatment with phenytoin (PHT) or valproate (VPA), SE refractoriness and hospitalisation length. Uni- and multivariate analyses of these factors were used to evaluate a dichotomised outcome: a positive outcome was defined as overall survival with response to benzodiazepines (BZD) and i.v. VPA or PHT.

Results: There were 106 patients (57 women, 49 men) with a mean age of 64 y (19.7–92.3) who had 111 episodes of SE. Hospitalisation length was 18 ± 15 d and mortality 11.3%. There were 18.9% convulsive SE (CSE), 34.2% subtle SE (SSE) and 46.9% non-convulsive SE (NCSE). Hospitalisation lasted longer in women (22 ± 16 d) than in men (13 ± 13 d), p = 0.001. Median SE duration was 48 h (1–408). Univariate analysis showed that patients >70 years had a higher chance of a positive outcome (OR: 5.14; p = 0.003), and patients with a negative outcome were younger (59 ± 15 vs 68 ± 15 y; p = 0.002). Patients with CSE had less frequently negative outcomes than those with SSE or NCSE (p = 0.008). Odds for a positive outcome in patients with SSE was reduced when compared with NCSE (OR: 0.323; p = 0.013). Hospitalisation length was increased in presence of a negative outcome (14 ± 11 vs 22 ± 17 d; p = 0.014), whereas SE duration between a positive or negative outcome was borderline significantly different (49 ± 52 vs 103 ± 116 h; p = 0.058). In a multivariate analysis young age was a risk factor for a negative outcome (OR: 1.037 [1.006–1.069] per 1 year less in age; p = 0.019) as well as SSE when compared to NCSE (OR: 3.802 [1.316–10.989]; p = 0.014) and to CSE (OR: 3.413 [0.935–12.50]; p = 0.06). There was an indication of a higher risk of a negative outcome in patients treated with PHT compared to VPA (OR: 2.59 [0.840–8.00]; p = 0.098).

Conclusions: NCSE and SSE were more prevalent in this retrospective analysis of a cohort of patients with SE at one tertiary care centre in contrast to epidemiological studies where CSE is the most frequent type of SE. In this hospital setting age <50 was associated with a higher risk for refractory SE (RSE), and age >70 with a higher chance to stop SE with BZD and i.v. PHT or VPA. NCSE and SSE carried a higher risk to become RSE.

Does cognitive impairment in Parkinson's disease predispose to the dopamine dysregulation syndrome?

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Objective: To evaluate the association of cognitive impairment and the dopamine dysregulation syndrome (DDS) in non-demented Parkinson's disease (PD) patients.

Background: Compulsive intake of dopaminergic medication and its associated motor, mental and behavioural complications define DDS which can lead to significant psychiatric co-morbidities and social consequences. The pathogenesis and risk factors of DDS remain partially unknown. Dysfunction of the prefrontal cortex has been linked to difficulties in decision taking and in foreseeing the consequences of one's own actions which facilitate risk-taking and novelty-seeking behaviour, also observed in DDS, and predispose to substance abuse. Cognitive impairment is prevalent in PD and primarily affects fronto-executive functions.

Methods: Fifty-seven non-demented PD patients were prospectively investigated. In a neuro-psychiatric assessment eight patients fulfilled published criteria of DDS. PD patients with DDS had a longer duration of disease and dopaminergic therapy, but otherwise did not differ in demographic and clinical findings. Comprehensive neuropsychological assessment included Stroop Interference Test, Goldenberg Association Learning, word (phonemic) and figural fluency (Five-Point Test), Rey Auditory Verbal and Visual Design Learning Test (RAVLT and RVDLT), Rey Complex Figure Test and an evaluation for other cognitive deficits.

Results: PD patients with DDS showed more difficulties in concept learning and shifting and in delayed recall of a complex figure than those without DDS, but did not differ in all other tests of fronto-executive functions, memory and visuo-spatial abilities. Also, no apraxia, visuo-perceptual or other cortical deficits were found in either group. Compared to age-matched healthy controls non-demented PD patients with and without DDS showed mild impairment in memory, executive and visuo-constructive functions.

Conclusion: These findings suggest a more marked impairment of fronto-executive functions in PD patients with DDS, which may represent a risk factor, but cannot confirm a significant association of DDS with cognitive decline.

Gait dysfunction and REM-sleep behaviour disorder in Parkinson's disease: is there an association?

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Objective: To evaluate the association of REM-sleep behaviour disorder (RBD) and gait dysfunction in Parkinson's disease (PD).

Background: Gait difficulties are frequent in PD, and even in an early stage irregular step timing can manifest, indicating impaired periodic locomotor activity. Animal and human studies indicate a possible periodic activity generator in the pedunculopontine nucleus (PPN) and its linked nuclei in the mesencephalic and pontine tegmentum. These nuclei have been shown to mediate locomotion and sleep and their degeneration in PD to lead to gait difficulties and RBD. A possible association remains to be determined.

Methods: Twenty-five patients with polysomnography (PSG)-confirmed (n = 12) or excluded (n = 13) RBD with mild to moderate PD (HY 2–3) and 20 age-matched healthy subjects were prospectively investigated. Gait analysis was performed at preferred and at a reduced speed under a rhythmic constraint on a split-belt treadmill with force sensors.

Results: PD patients walked slower than control subjects, but step frequency and duration were similar. Stride-to-stride variability was significantly larger in PD indicating ir-

regular step timing. No differences were found comparing PD patients with and those without RBD.

Conclusion: These findings confirm an impaired periodic locomotor activity in PD, but not the association with the presence of RBD, which may indicate separate neural circuits involved in gait control and generation of RBD.

Visual symptoms in Parkinson's disease

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Background: Persistent visual complaints are common in Parkinson's disease (PD). They remain underdiagnosed and are distressing. The detection of visual hallucinations is important for differential diagnosis and patient management. Recurrent visual hallucinations are a core diagnostic feature for Parkinson's disease dementia and may indicate disease progression in PD.

This study aims to (a) establish the prevalence of visual symptoms in PD and age-matched controls, (b) to assess risk factors associated with visual hallucination in PD and (c) to measure validity and reliability for North-East-Visual-Hallucinations-Interview (NEVHI) in PD.

Methods: Cross-sectional study including 90 community-based PD patients from the movement disorder clinics in Newcastle and Gateshead and 90 age- and gender-matched controls recruited from the local Age Concern Charity. Visual symptoms were assessed using NEVHI and a visual symptom check list, screening for blurred vision; double vision; reading difficulties; impaired spatial judgement and freezing induced by visual obstacles.

Results: Visual complaints were more prevalent in PD patients than in controls. Freezing induced by visual obstacles was only observed in PD patients (38%) but not in controls ($p < 0.001$). Recurrent complex visual hallucinations and illusions in the month prior to the assessment were reported in 31% of PD patients ($p < 0.001$). The prevalence of "feeling of presence" in isolation was not different in patients and controls. Patients with recurrent visual hallucinations were more impaired in activities of daily living than those without hallucinations. Informants tended to underreport visual hallucinations.

Conclusions: The NEVHI was helpful when assessing visual hallucinations in PD patients. Visual complaints and recurrent visual hallucinations are common in PD, especially in patients with impaired activities of daily living. Other visual symptoms are less specific for PD and can also be observed in controls. A reliable and valid measure for visual symptoms in PD is required.

Poster SNG

P 01 Chronic cerebral hypoperfusion and carotid stenosis

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Background: Carotid artery stenosis (CAS) is associated with the occurrence of acute ischaemic lesions that alter apparent diffusion coefficient (ADC) values in diffusion-weighted MRI (DWI). There are few data on chronic perfusion secondary to CAS and ADC measures.

Objective: Our hypothesis was to find increased ADC values in ipsilateral hemisphere of the CAS compared to the contralateral one in patients with symptomatic and asymptomatic CAS.

Methods: 20 symptomatic patients, 20 asymptomatic patients. Degree of stenosis between both groups was not significantly different. ADC values measured with DWI-MRI on both hemispheres (ipsilateral and contralateral to the stenosis). Regions of interest (ROI) were the anterior and posterior watershed regions (WsR), thalamus and occipital white matter.

Results: ADC values were significantly higher ($p < 0.005$) in the ipsilateral hemisphere in both WsR (anterior WsR mean ADC = 820 ipsi / 802 contra and posterior WsR = 814 ipsi / 796 contra) compared to the contralateral side. ADC values of thalamus and occipital regions were not significantly different.

When ADC values were compared within the symptomatic group and within the asymptomatic group, only ADC values from the symptomatic remained significantly altered (and in both WsR; $p < 0.005$).

Conclusion: We first confirm an increase of ADC values in WsR in the ipsilateral hemisphere of CAS that would be related with chronic hypoperfusion. In contradiction with previous data, our subgroup analysis found a significant difference only for symptomatic patients that could not be explained by the degree of stenosis. We hypothesise that those differences might be due to less collaterals in the symptomatic group.

P 02 Detection and quantification of patent foramen ovale: no need for transcranial acoustic bone windows?

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Background and purpose: Paradoxical thrombotic embolism via right-to-left cardiac shunt (RLS) is a risk factor for ischaemic stroke. Even younger patients may have insufficient transcranial acoustic bone windows. We thus studied prospectively if the detection and quantification of cardiac right-to-left shunt (RLS) due to patent foramen ovale could be done in acute stroke patients via the internal carotid artery (ICA) and via the vertebral artery (VA) as an alternative to transtemporal Doppler.

Methods: 85 collaborative patients subsequent to a recent stroke of unexplained origin in whom stenosis, occlusion or hypoplasia of the neck vessels has been excluded, underwent RLS detection using transtemporal Doppler 2 MHz (TTD). In addition, in 42 of them, Doppler detection of RLS was done via the distal VA (DVA) and in 43 this was done via the submandibular ICA (DICA). Artificial high-intensity signals (HITS) produced by a 1 ml/air – 9 ml/saline injection at rest and after efficient Valsalva's manoeuvre (VM) were measured by the sonographers blinded to the results of TTE/TEE. The two methods were compared in terms of number of HITS. For more than 60 HITS or "curtain effect" the number 60 was given.

Results: 78 patients (40 VA; 38 ICA; 56 men; mean age 50.9 y) were retained. In the remaining 7 patients (2 DVA; 5 DICA), breathing artifacts during VM did not allow to evaluate RLS. TTD, DVA and DICA had a 100% agreement as to absence of HITS (39 patients). Pearson Correlation between the number of HITS of TTD and DVA was significant at rest ($p < 0.0003$) and after VM ($p = 0.0005$), and of TTD and DICA was also significant at rest ($p < 0.0005$) and after VM ($p < 0.0005$).

Conclusion: Doppler ultrasound via the distal VA or the submandibular ICA could be an alternative in the detection and grading of RLS in patients with poor transcranial bone windows.

P 03 Fatigue and excessive daytime sleepiness in multiple sclerosis

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Objective: To assess frequency and severity of fatigue and excessive daytime sleepiness (EDS) in patients with multiple sclerosis (MS), and to study their relation to disease duration and severity, as well to depression.

Background: Fatigue is one of the most frequent and disabling symptoms in MS. Little is known about the prevalence of EDS and its association with fatigue.

Patients and methods: We prospectively assessed Fatigue Severity Scale (FSS) scores, Epworth Sleepiness Scale (ESS) scores, Beck Depression Inventory (BDI) scores, as well as disease severity (estimated by the Expanded Disability Status Scale, EDSS) and duration in 442 consecutive patients with definite MS.

Results: Mean FSS score was 4.4 ± 1.6, mean ESS score was 7.6 ± 4.8. Fatigue (FSS score ≥4.0) was found in 276 (62.4%), EDS (ESS ≥10) in 144 (32.6%), and both com-

plaints in 122 patients (27.6%). Fatigue without EDS was found in 154 patients (34.8%), whereas EDS without fatigue was found in only 22 patients (5.0%). FSS and ESS did not correlate with disease duration (r = –0.07 and –0.09 resp., p = 0.16 and 0.07 resp.) nor with EDSS (r = 0.08 and 0.01 resp., p = 0.12 and 0.83 resp.). Both FSS and ESS were significantly related to BDI scores (r = 0.35 and 0.36 resp., p = 0.005 and 0.003 resp.). MS patients with both fatigue and EDS (n = 122) had a higher body mass index (BMI) (27.0 ± 5.9 vs 25.0 ± 4.6, p = 0.05) and higher BDI scores (14.8 ± 8.4 vs 8.7 ± 8.1, p = 0.03) than MS patients with only fatigue (n = 154).

Conclusions: Both fatigue and EDS are frequent complaints in MS and appear to be largely independent from disease duration and disability. If present, EDS most often occurs in combination with fatigue. The co-occurrence of the two symptoms is associated with higher BMI values and depression severity.

P 04 Idiopathic hypersomnia: a dopaminergic disorder?

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Background: Idiopathic hypersomnia (IH) is a disorder of unknown origin characterised by excessive daytime sleepiness (EDS) and prolonged non-refreshing sleep. No biological marker for IH is known. Dopamine is involved in a variety of brain functions including sleep-wake, reward and motor control.

Aims: To investigate the neurochemical background of IH.

Patients and methods: Seven untreated patients (5 female, 2 male; mean age: 34 years) fulfilling the international diagnostic criteria for IH underwent extensive sleep-wake studies. Dopamine transmission was assessed using positron emission tomography (PET): a radioligand for D_2 dopamine receptor, and 18-Fluorodopa (n = 3), a tracer for striatal dopamine uptake, were applied in two successive sessions. Ratio of the distribution volumes in striatum to that in occipital cortex was calculated. The results were compared to a normative data set of healthy controls. The association between EDS and D_2 receptor availability was explored by correlation analyses.

Results: All patients had EDS (Epworth score: 15.7 ± 3; mean ± SD), high sleep efficiency (95 ± 4%), short sleep latency (11 ± 6 min) and high amounts of slow-wave sleep (17 ± 5%) on PSG. Mean sleep latency on multiple sleep latency test (MSLT) was decreased (5.8 ± 2 min). CSF-hypocretin levels were normal (607 ± 254 pg/µl). Dopamine-receptor availability was increased in the putamen (z-scores left: 3.2 ± 1.3, right: 2.9 ± 0.9) and in the N. caudatus (right: 1.9 ± 0.5, left: 2.5 ± 0.7). Dopamine uptake was also increased in the putamen (right: 3.9 ± 0.6, left: 3.5 ± 0.2) but not in the N. caudatus (left: 1.9 ± 3.9; right: 0.6 ± 3.4). Mean sleep latencies on MSLT correlated with the increase of D_2 receptors in the putamen (Spearman's rho: 0.65, p = 0.01) and the N. caudatus (0.56, p = 0.04). Epworth scores showed an inverse correlation with D_2-receptors' availability in the N. caudatus (–0.56, p = 0.04).

Conclusion: Increased striatal availability of dopamine D_2 receptor and dopamine uptake indicate a dopaminergic upregulation in IH. These findings suggest the existence of a (first) biological marker IH and a potential new approach to its treatment.

P 05 Language network analysis in a ventriloquist with non-fluent primary progressive aphasia using fMRI

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Background: Primary progressive aphasias (PPA) include various combinations of naming and comprehension difficulties. There are no data concerning ventriloquist suffering from PPA.

Objective: Identify the neural substrate of language networks in a ventriloquist with non-fluent PPA.

Setting: Single-case study of a 67-year-old right-handed male ventriloquist who complained of oral speech difficulties and improvising or playing his favourite melodies on the accordion. Neurolinguistic examination disclosed slowed speech with slight anarthria, some rare echolalia and bucco-linguo-facial imprecisions. Verbal fluencies and Stroop test were abnormal. Naming, oral comprehension, repetition, writing and other instruments were all preserved. MRI and FDG-PET were compatible with non-fluent PPA.

Methods: Using an fMRI bloc design and a voxel-by-voxel analysis with SPM2, we examined different language tasks including rhyme detection, semantic categorisation (i.e. non-productive reading and comprehension), oral and "ventriloquist" picture naming and verb-generation tasks (i.e. language production).

Results: Non-productive tasks activated the left inferior frontal gyrus (BA 44/45/46) and superior temporal gyrus (BA 21/22, p <0.0001). Language-production tasks (including both oral and "ventriloquist" naming) activated a large perisylvian network including inferior frontal gyrus, dorsolateral prefrontal, superior temporal gyrus largely on the left hemisphere (p <0.0001). Oral versus "ventriloquist" naming showed a significant activation in the fronto-polar region on the left (x; y; z = –37; 58; 21; t = 7.47; p <0.0001 at voxel level).

Conclusion: Both oral and "ventriloquist" naming tasks activated a large network including classic language areas in the left hemisphere. The brain regions underlying oral naming with respect to the "ventriloquist" mode involved a very anterior portion of the left prefrontal cortex. This result is interpreted in terms of recruitment mechanisms to compensate a particular speech difficulty in this patient with non-fluent PPA.

P 06 Normal appearing white-matter pathology in MS – visualisation and quantitative assessment with Q-space analysis of the slow diffusion component

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Introduction: Histopathologic studies and several quantitative MR markers have indicated pathology in the normal appearing white matter (NAWM) in MS patients. However, it has been challenging to visualise this. We focused on this problem and employed Q-space imaging of the slow-diffusion component to detect NAWM changes and investigated a cohort of well-characterised MS patients.

Methods: We examined 71 MS patients (48 w, 23 m; mean DD = 15.6 years (3–38 years); mean EDSS = 3.2 (0–6.5) with various disease courses and 10 normal controls (NC) (5 w, 5 m) on a 3T Siemens ALLEGRA system. The standardised brain MRI protocol included transverse 5 mm T_2w-TSE, FLAIR and DWI including high b-value measurements for q-space analysis. DWI: 6 directions, 16 b-values in each direction, b-value range: b = 0 to b = 9021 s/mm^2 by linearly increasing the diffusion-gradient amplitude, delta/DELTA = 43/48 ms; TE/TR = 125/1450 ms, 128 × 128 matrix, voxel size = 1.875 × 1.875 × 5 mm^3. This sequence provided 8 axial slices centred at the level of the corpus callosum. Acquisition time for the whole DWI data set was 13 minutes. The NAWM was analysed on probability of zero displacement (PZD) maps and histogramm analysis.

Results: The mean white-matter PZD values of NC (1617 ± 43) differed significantly (p <0.005) to the PZD values of patients (1545 ± 63). A cluster analysis (allowing for 3 clusters; 1456 ± 50, 1547 ± 21, 1610 ± 24) demonstrated differences of 49/71 patients to NC, which closely matched the visual analysis identifying the same individuals showing pathology. There was no correlation of EDSS with mean NAWM PZD, T_1- or T_2-lesion volumes. An inverse correlation of PZD with T_1- or T_2-lesion volumes (cc = –0.61; –0.66) was found.

Conclusions: In this 3T study we used a protocol for clinical use of colour-coded PZD maps that were highly sensitive to detect reductions of the slow-diffusion component in the NAWM of MS patients. This was both

visually and quantitatively evident and underlines the usefulness of this imaging and analysis approach to detect otherwise covert pathology. Clinical characteristics were not predictive of the NAWM changes, and particularly in patients with only slight functional compromise (EDSS 0–2) additional MRI information on NAWM may be useful background information.

P 07 Sleepiness is not always perceived before falling asleep in young healthy totally sleep-deprived, elderly partially sleep-deprived subjects and in sleepy patients

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Objective: We prospectively evaluated the spontaneously perceived sleepiness (SPS) prior to sleep onset during Maintenance of Wakefulness Test (MWT) in totally sleep-deprived young subjects, in partially sleep-deprived elderly subjects and in sleepy patients.

Method: 28 young healthy students (mean age 22.4 years; 13 females) after a whole night-sleep deprivation, 11 elderly healthy subjects (7 males, mean age 60.5 years, ± 10.0 years) after 5 instead of >7 hours sleep and 159 patients (mean age 39.8 years; 59 females) with sleepiness of various origins underwent 4 MWT trials. They received the instruction: "Indicate your earliest symptoms of sleepiness and try to stay awake as long as possible!" Overt sleep (OS) and microsleeps (MS) of at least 3 seconds' duration were scored separately.

Results: Overall 17 of 28 young healthy subjects (60.7%), 4 of 11 elderly healthy subjects (36%) and 64 of 159 patients (40.3%) presented either an MS or an OS fragment before indicating SPS at least in one of 4 MWT trials. This outcome did not change when participants were awarded a payment for signalling their sleepiness timely. In both, young healthy subjects as well as patients, females demonstrated a better awareness of SPS than male subjects.

Conclusion: The relatively frequent occurrence of falling asleep before signalling sleepiness, now also shown in elderly subjects, is in sharp contrast to the general assumption that nobody can fall asleep without prior awareness of sleepiness. If these results are confirmed in larger series or in any driving situation, far-reaching consequences will ensue: (1) The simple advice to sleepy subjects that they should not drive when sleepy would no longer be adequate. (2) Motor-vehicle crashes due to microsleeps could no longer be judged as due to "reckless driving" in all cases. (3) Prevention strategies against sleepiness-induced motor-vehicle crashes would have to include efforts to improve perception of SPS.

P 08 Autologous stem-cell transplantation as therapeutic option of therapy-resistant CIDP

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A 58-year-old woman had a 5-year history of chronic inflammatory demyelinating polyneuropathy (CIDP). Clinically, she showed tetraparesis with distal predominance in upper and proximal predominance in lower extremities, bulbar affection with dysphagia and double vision and only mild sensory disturbances. Diagnosis was confirmed by electrophysiological studies. Initially, she responded well to intravenous immunoglobulins (IVIG) but then relapsed. Therapy with steroids was ineffective. Under cyclosporine the patient was clinically stable but developed renal insufficiency, therefore the dose had to be reduced. Azathioprine was not tolerated due to leukopenia. At the time of admission therapy consisted in cyclophosphamide, repetitive plasmapheresis and mabthera monthly. She responded to this therapy, although efficacy was of short duration and symptoms relapsed frequently. Considering the therapy resistance and the response to an immunomodulating therapy, we decided to perform an autologous stem-cell transplantation (ASCT) according to a phase-II joint pilot study of autologous peripheral blood progenitor cell transplantation with the King's College London School of Medicine. The patient tolerated ASCT well and regained full strength after the transplantation. Until now (4 months post transplantation), she is free from relapses and needs no medication. This is to our knowledge the first case of therapy-refractory CIDP treated with ASCT in Switzerland and clinical data are so far promising.

P 09 Cognitive and sleep EEG evolution after paramedian thalamic stroke – preliminary results

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Introduction: Functional recovery after stroke is dependent on the adaptive plasticity of the human brain. There is strong evidence that sleep essentially contributes to the processes of brain plasticity and learning. The exact link between sleep, EEG and cognition in stroke recovery remains unclear.

Aim: To investigate the relationship between sleep and stroke recovery by (1) comparing EEG power in the slow wave (SWA) and spindle frequency ranges (SFR) in the acute phase after stroke, 3 and 6 months later, (2) correlating these EEG parameters to behavioural changes during the recovery process.

Patients and methods: Seven patients, two with bilateral paramedian thalamic stroke (PMTS) and five with unilateral PMTS underwent high-density EEG (hd-EEG) examination with 128 electrodes during sleep. Additionally, executive functions, attention and memory were assessed. Three patients were tested in the acute phase after stroke, 3 and 6 months later, one patient in the acute phase and after 3 months and three patients only in the acute phase.

Results: Both patients with bilateral PMTS presented with hypersomnia, severe attention deficit and mild memory impairment in the verbal and figural domains. In hd-EEG both SWA and sleep SFR were recorded in typical locations without gross asymmetry; power in SFR was very low. After 3 and 6 months improvement of the hypersomnia and all behavioural tests but no difference in SFR were found in one of the patients. In the other patient only slight improvement of the hypersomnia and the behavioural tests were observed, power in SFR recovered. In the five patients with unilateral PMTS no cognitive impairment or attention deficit was found and power in SFR was preserved.

Conclusion: Behavioural and EEG changes occurred only after bilateral PMTS. Power in SFR was dramatically decreased in the acute phase after bilateral PMTS but not after a unilateral lesion. Recovery of power in SFR occurred only in the patient with slight clinical improvement.

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P 10 Confocal live imaging reveals contribution of CD8$^+$ T cells to demyelination and axonal damage

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Multiple sclerosis (MS) is the most common chronic inflammatory and often disabling disease of the central nervous system (CNS). Apart from loss of myelin and oligodendrocytes, axonal damage is considered to be the cause of permanent neurological impairment. Perivascular lesions containing T cells, macrophages, B cells and immunoglobulin as well as complement deposits represent hallmarks in MS pathology. Yet, it remains unclear which immune cells and effector mechanisms are most relevant for eliciting CNS damage in MS.

We have therefore established an organotypic CNS slice culture system allowing us to dissect the pathogenic effects exerted by different immune cells individually or in defined combinations. Using confocal life imaging, we were able to directly monitor T cell/CNS interaction in slices derived from PLP-GFP transgenic mice. Our results suggest that antigen specific $CD8^+$ T cells may directly transect myelinated axons. This damage seems to be restricted to an environment where specifically stimulated T cells recognise their corresponding antigen. We further observed that only stimulated T cells move with varying dynamics, whereas unstimulated T cells remained immobile. The movement of stimulated T cells increased if the specific antigen was present, leading to a massive invasion of T cells into the slice.

Our data strongly suggest that $CD8^+$ T cells may contribute to CNS damage in MS. Furthermore, this injury seems to result from antigen specific CNS-immune interactions directed to the myelin sheath causing nonspecific "collateral" bystander damage to the myelinated axon.

P 11 Deficient high-acceleration vestibular function in polyneuropathic patients

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Background: Unsteadiness during standing and walking is a frequent complaint of patients with polyneuropathy (PNP).

Objective: To determine whether balance disorders in PNP patients are caused by reduced proprioceptive input from the feet alone or whether reduced vestibular input, resulting from involvement of the vestibular nerve, may be an additional factor.

Methods: 37 patients (age: 65 years ± 12 SD; 12 females) with electro-diagnostically confirmed PNP (predominantly axonal: 18; predominantly demyelinating: 19) underwent horizontal search-coil head impulse testing, which assesses the high-acceleration vestibulo-ocular reflex (VOR).

Results: Relative to a healthy comparison group, the gains (eye velocity divided by head velocity) of the horizontal VOR were reduced in 27 of 37 patients (unilateral: 13; bilateral: 14). The percentages of patients with unilateral or bilateral VOR deficits were not significantly different between patients with axonal or demyelinating PNP (chi square test: $p > 0.05$). The occurrence of VOR deficits was independent of the time elapsed since PNP diagnosis.

Conclusions: Two thirds of patients with axonal or demyelinating PNP show unilateral (~50%) or bilateral (~50%) gain reductions of the horizontal high-acceleration VOR. This suggests that imbalance in these patients is multisensory, i.e. both proprioceptive and vestibular. Such information is highly relevant for subsequent physical therapy, since vestibular exercise improves balance control and reduces disability.

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P 12 EEG in the detection of the beginning psychosis

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Background: EEG investigation in patients with an At Risk Mental State (ARMS) for psychosis and patients with a first episode of psychosis (FE) in comparison to healthy controls (HC) in a clinical follow-up study of Early Detection of Psychosis.

Methods: Seventy-three patients (42 ARMS, 31 FE) and 35 HC were investigated. ARMS patients were followed up in order to monitor transition to psychosis. Psychopathology was assessed with respect to positive and negative symptoms. At study baseline EEG was recorded using the 10/20 system. Two blinded neurologists analysed the EEGs visually for presence of generalised or focal slowing and epileptiform discharges. EEG data were controlled for medication and substance abuse. For statistical analyses we used Chi-square tests, logistic regression, ANOVA and receiver-operating characteristics (ROC).

Results: Patients showed significantly more pathological EEG abnormalities located more frequently in temporal or frontotemporal regions ($p < 0.01$) of the brain than healthy controls ($p < 0.05$), with twice as many pathologies in ARMS than in FE patients. A pathological EEG was significantly associated with a decreased risk for transition to psychosis. The predictive specificity of psychosis could be enhanced from 59 to 73% by considering EEG pathology in addition to psychopathology alone.

Conclusion: These results show that EEG investigation in patients suspected for psychosis can be supportive in the identification of patients who will develop psychosis later on.

P 13 Evaluation of paradoxical embolism in patients with cryptogenic ischaemic stroke and patent foramen ovale

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Background: Several studies have suggested a possible relationship between patent foramen ovale (PFO) and cryptogenic ischaemic stroke. However, optimal management of patients with cryptogenic stroke and PFO remains unclear. Detection of concurrent deep venous thrombosis (DVT) and/or pulmonary embolism may be helpful in determining paradoxical embolism as stroke aetiology and guiding treatment decisions.

Methods: 728 consecutive patients with ischaemic stroke were analysed retrospectively. Stroke aetiology was classified according to modified TOAST criteria. Patients with cryptogenic stroke were analysed for the evaluation of PFO, DVT and pulmonary embolism.

Results: Stroke aetiology was cryptogenic in 165 patients (22.7%). Evaluation for PFO was performed in 112 patients (67.9%), and PFO was found in 69 patients (61.6% of evaluated patients). Clinically, DVT or pulmonary embolism was not suspected in any patient. Among the 69 patients with PFO, venous thrombosis was evaluated in 58 and confirmed in 12 patients (diagnostic yield: 20.7%), pulmonary embolism was evaluated in 46 and confirmed in 7 patients (diagnostic yield: 15.2%).

Conclusion: In 13 of 69 patients with cryptogenic ischaemic stroke, PFO and no clinical suspicion of DVT or pulmonary embolism, either DVT, pulmonary embolism or both were detected. Routine evaluation of DVT and pulmonary embolisms yielded a considerable rate of treatment-relevant findings and may be helpful in guiding decision for invasive treatment of PFO.

P 14 Excellent steroid response of inflammatory cerebral amyloid angiopathy: a case report

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Background: Patients with cerebral amyloid angiopathy (CAA) may rarely present with subacute encephalopathy. Pathological examination demonstrated perivascular inflammation in these cases, suggesting that immunosuppressive treatment may be effective.

Case report: A previously healthy 76-year-old female patient presented in the emergency department with a 10-day history of gradual cognitive decline, blurred vision and light headedness. Minimental score (MMS) was 21. On examination she showed right homonymous hemianopia, mild rigidity and tremor. T_2-weighted brain MRI demonstrated widespread bihemispheric confluent white-matter lesions with petechial haemorrhages, left more than right, without contrast enhancement. An extensive work-up including CSF examination (with negative PCR for JC virus) was unremarkable. In the following days she further declined cognitively (MMS 17). Due to the risk of bleeding stereotactic biopsy was not performed. She was treated with prednisone 50 mg for 4 weeks with full recovery of her mental status (MMS 30) and

impressive resolution of white-matter abnormalities.

Conclusion: The diagnosis of inflammatory CAA was made based on a rapidly progressing encephalopathy with highly suggestive MRI findings, being almost completely reversible under corticosteroids. This is an instructive case, because it demonstrates that the inflammatory subtype may be a treatable form of CAA.

P 15 Functionnal investigation of a peduncular-like hallucinosis in the absence of midbrain damage

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Background: Peduncular hallucinosis (PH) mainly occurs after midbrain, pontine and thalamic strokes. To our knowledge, cortical stroke produces release, but not PH.

Case report: An 83-year-old man was admitted for vivid and continuous complex visual and auditory hallucinations, characterised by panoramic scenes of helicopters and a large river with bathing crowd, accompanied by liturgical songs. They increased when the patient looked at a blank wall and disappeared at eye closure. Only initially were these hallucinations criticised by the patient.

Clinical investigations: Visual acuity was of 60% and visual field was intact. Neuropsychological evaluation showed an MMSE-score of 23 and poor memory. MRI revealed no brain-stem lesions, but a chronic left parietal stroke. EEG showed no epileptic activity. We performed a bloc-design fMRI experiment, using 5 periods of alternating visual stimulation (VS) of 24 s with a checkerboard (to stop PH) and a blank screen (resting [R]) of 24 s, to allow PH. VS compared to R dominantly activated bilateral visual areas. More interestingly, R versus VS showed a complex pattern of activation involving posterior cingulate cortex, SMA, left superior temporal gyrus and inferior parietal lobule.

Conclusion: This case addresses the question of peduncular-like hallucinosis in extra midbrain lesion. The symptomatology presented here meets all characteristics of the PH without any lesion in the brainstem or the thalamus. fMRI results suggest that the internally generated vivid and complex scenes in the patient's brain are subtended by large neural networks that not necessarily imply the midbrain.

P 16 Behandlung akuter Migräneanfälle mit Eletriptan: Ergebnis einer Kohortenstudie aus Schweizer Arztpraxen

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Eletriptan gehört mit Almotriptan und Rizatriptan zu den von Migränepatienten, Hausärzten und Neurologen bevorzugten Triptanen. Ziel des Projekts war es, eigene Erfahrungen mit Eletriptan 40 bzw. 80 mg im Alltag von Schweizer Arztpraxen bzw. Ambulanzen zu sammeln.

Methodik: Nach Genehmigung des Protokolls durch die kantonalen Ethikkommissionen und schriftlichem Einverständnis wurden Patienten, die mindestens einen mässigen oder starken Migräneanfall mit oder ohne Aura in den vorausgehenden 6 Wochen hatten, eingeschlossen. Sie nahmen innerhalb von 4 Stunden nach Beginn des Anfalls Eletriptan 40 mg (Visite 1, 2) oder 80 mg (Visite 3, 4). Eine 2. Eletriptan-Dosis nach 4 Stunden oder Rescue-Medikation (RM) war erlaubt. Behandlungszeitraum: 4 Migränezyklen, max. 16 Wochen. Hauptzielkriterium: die Kopfschmerz (KS)-Response nach 2 Std (4-Punkte-Skala, gemäss Definition). Darüber hinaus wurden 15 Nebenzielkriterien erhoben. ITT («Last Value Carried Forward») Analyse.

Ergebnisse: 207 Patienten wurden aufgenommen, 184 beendeten die Studie. Bei weniger als 25% der Patienten kam es zum Wiederauftreten von KS (seltener unter Eletriptan 80 mg). Die Behandlungszeit betrug 4 Tage (Median). Bis zu 18% nahmen RM, im Median aber erst nach 34 Std. Beim ersten Migräneanfall betrug die KS-Response 62% (unabhängig von der Eletriptan-Dosis), nach 4 Std 76% und nach 24 Std 84% (entsprechende Response bei den anderen Migräneanfällen). Komplette Response wurde bei bis zu 50% der Patienten erzielt, funktionelle Response bei etwa 65%. Schmerzintensität und Schwere der KS besserten sich innerhalb von 24 Stunden zunehmend, ebenso die Migräne-assoziierten Beschwerden. Die meisten Patienten waren nach 24 Stunden schmerzfrei, unabhängig von der Dosis zu 60% im 24-Stunden-Intervall. 59 Patienten klagten über 105 unerwünschte Ereignisse, 10 Patienten über 16 schwere, von denen 14 in Zusammenhang mit Eletriptan standen.

Schlussfolgerung: Das Ergebnis steht im Einklang mit den bereits publizierten Ergebnissen zur guten und schnell einsetzenden Wirksamkeit von Eletriptan und seiner guten Verträglichkeit, auch bei Anwendung über mehrere Monate.

P 17 Hereditary diffuse leukoencephalopathy with spheroids (HDLS) – an uncommon cause of frontotemporal dementia

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Background: HDLS is a rare autosomal dominant disorder characterised by cerebral white-matter degeneration with axonal spheroids. The genetic basis of HDLS is still unknown. We present 3 patients of a two-generation family with HDLS manifesting as a frontotemporal dementia.

Methods: The index patient and her brother underwent neurological and neuropsychological examinations as well as extensive laboratory testing, electroencephalography (EEG), magnetic resonance imaging (MRI) and positron emission tomography (FDG-PET). Available medical records from the mother were reviewed. Brain autopsy was performed in the index patient.

Results: All patients had a progressive frontotemporal dementia with behavioural and cognitive symptoms with disease onset ranging from 38 to 46 years and disease durations of 2, 8 and 11 years. The index patient, however, manifested with progressive gait apraxia and developed additional ideatoric, ideomotoric and ocular apraxia. No apraxia or gait disorders were noted in the other patients. The index patient and her brother had generalised epileptic seizures in late disease stages. EEG showed no specific alterations. Cerebral MRI revealed cortical atrophy with frontotemporal predominance and subcortical leukoencephalopathy and FDG-PET demonstrated decreased FDG uptake in parietal and frontal regions. Brain pathology revealed pronounced diffuse leukoencephalopathy with secondary astrogliosis and spared U-fibres. Abundant axonal spheroids were present in affected white-matter areas and in a much lesser extent in the overlying cortex thus confirming the diagnosis of HDLS.

Conclusions: HDSL has to be considered as a cause of frontotemporal dementia, in particular if neuroimaging reveals white-matter lesions. Our observations demonstrate a remarkable intrafamiliar phenotypic variability as well as a long disease course compared to the literature.

P 18 Is cognitive impairment in Parkinson's disease associated with REM-sleep behaviour disorder?

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Objective: To test whether REM-sleep behaviour disorder (RBD) in non-demented patients with Parkinson's disease (PD) is associated with cognitive impairment.

Background: Cognitive impairment is prevalent in PD and may progress to dementia. Recent studies have found an association of RBD with cognitive impairment in PD which could, thus, represent a risk factor for future cognitive decline.

Methods: Thirty-four non-demented PD patients with polysomnography (PSG)-confirmed (n = 14) or excluded (n = 20) RBD were prospectively investigated (table 1). Comprehensive neuropsychological assessment included Stroop Interference Test, Goldenberg Association Learning, word (phonemic) and figural fluency (Five-Point Test), Rey Auditory Verbal and Visual Design Learning Test (RAVLT and RVDLT), Rey Complex Figure Test and an evaluation for other cognitive deficits.

Results: PD patients with RBD presented more verbal learning impairment and visuoconstructive difficulties than those without RBD, but otherwise they performed alike in neuropsychological testing (table 2). Compared to age-matched healthy controls PD patients with and without RBD showed mild impairment in memory, executive and visuoconstructive functions.

Conclusion: These findings cannot uniformly confirm an association of cognitive impairment with the presence of RBD in PD. An association may reflect a more widespread neurodegeneration having progressed beyond the brainstem which has been linked with the generation of RBD. A longitudinal study can verify whether RBD in PD predicts future cognitive decline.

P 19 Isolated left ventricular non-compaction: a rare cause of stroke

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Background: Isolated left ventricular non-compaction (ILVNC) is a rare congenital cardiomyopathy due to intrauterine compaction arrest of the myocardial fibre meshwork. Although the abnormal wall architecture with abundant intertrabecular recesses is highly propitious to thrombus genesis, initial symptoms leading to diagnosis in adult patients mostly concern the heart. Conversely, stroke caused by ILVNC remains infrequent with only individual cases reported in the literature.

Case report: We describe a case of a 38-year-old man who presented, as a first manifestation of ILVNC, a cardio-embolic stroke in the territory of the right medial cerebral artery. Diagnosis was made by echocardiography and therapeutic anticoagulation was introduced. However, due to non-compliance, the patient did not take his medication during a few days, which led to a second and more extensive stroke affecting the same vascular territory.

Conclusion: This case should highlight the necessity of performing wide aetiological investigations after a stroke in young adults and the importance of strict therapeutic anticoagulation, once the diagnosis of ILVNC has been made.

P 20 Mapping impaired functional connectivity in patients with focal brain lesions: an MEG study

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Background: Functional maps of eloquent brain regions are increasingly used during surgical planning in patients with brain lesions, but their accuracy can depend on patient cooperation and on study paradigms that are capable of reliably activating the brain area of interest. We propose to map non-functional, necrotic or structurally disconnected brain areas according to their decreased functional connectivity with intact regions.

Methods: Magnetoencephalographic (MEG) recordings of cortical activity were obtained from 15 consecutive patients with focal brain lesions and from 14 healthy controls during resting state. Neural activity in the brain was reconstructed using an adaptive spatial filtering technique. The imaginary component of the complex valued coherence was calculated for pairs of brain voxels and used as an index of their functional connectivity.

Results: The alpha frequency range corresponding to the human cortical idling rhythm showed the greatest imaginary coherence magnitude in all subjects. In healthy subjects eloquent brain areas had greater alpha coherence than non-critical areas. When compared to healthy controls, all patients with focal brain lesions had diffuse or scattered brain areas with decreased alpha coherence. Patients with lesion-induced neurological deficits displayed decreased connectivity estimates in the corresponding brain area compared to intact contralateral regions. In patients with tumours who did not have preoperative neurological deficits, brain areas showing low coherence could be surgically resected without the occurrence of postoperative deficits.

Conclusion: Resting state coherence measured with MEG is capable of mapping the functional connectivity of the brain and can be used for imaging damaged vs intact tissue.

P 21 Methionine metabolism in an animal model of septic encephalopathy

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Background: Sepsis is a disease with a high incidence and a high lethality. Septic encephalopathy is a brain dysfunction secondary to sepsis, which occurs in up to 70% of septic patients and has been found to be associated with a significantly higher mortality. The aetiology of septic encephalopathy is unknown. Sepsis is accompanied by profound metabolic disturbances. In mammalian methionine metabolism S-adenosylmethionine (SAM) is produced, which is important for the synthesis, e.g., of neurotransmitters and glutathione, and SAM acts as an anti-inflammatory agent. Degradation product and antagonist of SAM is S-adenosylhomocysteine (SAH). This study investigated changes in this metabolism during sepsis in a rodent model.

Methods: Sepsis was induced in male Wistar rats (n = 21) by an intraperitoneal injection of bacterial lipopolysaccharide (LPS, 10 mg/kg). Controls (n = 18) received the vehicle only. 24 hours after injection 1 ml blood was collected by cardiac puncture. Puncture of the suboccipital fossa was performed to collect cerebrospinal fluid (CSF). Methionine metabolites were measured by using stable isotope dilution tandem mass spectrometry. Plasma total homocysteine and cysteine were measured by HPLC using fluorescence detection. Glutathione was assayed by a modified enzymatic microtitre plate assay.

Results: We observed significantly higher plasma levels of SAM ($p < 0.001$) and of the ratio of SAM/SAH ($p = 0.004$) in septic animals. In cerebrospinal fluid septic animals also had higher levels of SAM for trend ($p = 0.067$). Oxidative stress was reflected by an increase in the ratio of oxidised/reduced glutathione in septic animals ($p = 0.001$).

Conclusions: Sepsis is associated with an increase in the SAM/SAH ratio in plasma and CSF in rodents. This indicates an altered methylation potential during sepsis, which may be relevant for sepsis-associated impairment of transmethylation reactions, circulation and defence against oxidative stress and contribute to the aetiology of septic encephalopathy. If verified in humans, such findings could lead to novel strategies of supportive treatment of sepsis, as methionine metabolism can easily be manipulated by dietary strategies.

P 22 Modulations of the somatosensory vertical in the roll plane

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Whole-body roll dependent deviations (roll underestimation = a-effect; roll overestimation = e-effect) of subjective visual vertical (SVV) relative to earth verticality and increases of intra-individual SVV variability with increasing body roll have been reported. Since non-visual tasks showed significantly smaller or even absent errors in roll positions up to 40° (Wade SW and Curthoys IS, The effect of ocular torsional position on perception of the roll-tilt of visual stimuli. Vision Res. 1997;37[8]:1071–8), it has been postulated that a- and e-effects are a consequence of imperfect central processing of visual information. Here we measured the somatosensory vertical (SSV) in six right-handed healthy humans. They were asked to adjust with their right hand a rod along the perceived earth-vertical while being in stationary whole-body roll positions (upright, 45°, or 90° right- and left-ear down). In all roll orientations tested, average SSV errors were not significantly different from zero. Variability was minimal in upright (3.6 ± 1.5°) and increased with increasing roll to either side up to 11.8 ± 6.9° (at 90° left-ear down). Since no significant SSV deviations were found for roll angles up to 90°, we can confirm the previous work by Wade and Curthoys. Since the a- and e-effect seem to be task-dependent, we consider imperfection in central processing and integration of visually based estimates of vertical more likely than an erroneous graviceptive signal. For the clinical purpose of evaluating the integrity of the peripheral and central vestibular systems involved in verticality perception, using the SSV instead of the SVV helps avoiding confounding effects induced by the a- and e-effect.

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P 23 Motor cortical plasticity and EEG spectrum after focal brain ischaemia in the rat

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Promotion of neuronal plasticity may represent a new perspective for effective medical interventions after ischaemic stroke. Clinical and experimental data suggest that sleep may play a role in mediating neuronal plasticity after ischaemic brain injury. To test this hypothesis, correlates between sleep, EEG power spectra and motor function recovery were investigated in a rat ischaemia model.

Cortical ischaemia was induced in 8 male Sprague-Dawley rats by coagulating the distal middle cerebral artery (MCA), 8 sham-operated rats formed a control group. EEG was recorded over the motor cortex (M1). Power spectra were calculated for EEG during slow-wave sleep, paradoxical sleep and wakefulness. Motor function was assessed by single-pellet reaching.

Coagulation of the MCA resulted in a small infarct in the somatosensory cortex. Success on the pellet reaching task was reduced by at least 25% in ischaemic animals. EEG power over the M1 region showed a marked reduction in the 12–25 Hz beta frequency band in the ischaemic hemisphere. The reduction in beta power was present in all vigilance states, but was greatest during paradoxical sleep. The performance in pellet reaching and the EEG parameters tended towards normal during a recovery period of 30 days.

The results suggest that high frequency EEG may reflect neuronal plasticity in the sensorimotor cortex after stroke.

P 24 Multiple sclerosis is not linked with a dysregulated cytokine T-cell response against Epstein-Barr virus

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We have previously shown that there was an enrichment in highly differentiated ($CCR7^-$) $CD8^+$ T cells in the cerebrospinal fluid of patients with early multiple sclerosis (MS). We have also found that the same category of patients had a high Epstein-Barr virus (EBV)-specific, but not an increased cytomegalovirus (CMV)-specific, $CD8^+$ T-cell response in the blood, suggesting that EBV might be involved in the pathogenesis of MS.

We decided to explore whether this increased EBV-specific $CD8^+$ T-cell response in early MS patients was related to a dysregulated cellular immune response against this virus. For this purpose, we studied the mRNA expression of different cytokines that are considered to be relevant in MS after EBV or CMV stimulation of T cells in MS patients and healthy controls (HC). T cells were discriminated between naive and central memory ($CCR7^+$) on one hand, and effector memory and effector T cells, thus highly differentiated T cells ($CCR7^-$), on the other hand.

Except for an increased IFN-gamma mRNA expression by EBV-stimulated highly differentiated ($CCR7^-$) $CD8^+$ T cells, we did not find a different cytokine mRNA expression pattern between MS and HC after EBV stimulation, suggesting that the increased frequency of EBV-specific $CD8^+$ T cells found in the blood of MS patients is not linked with a dysregulated T-cell response against EBV.

P 25 Neurorehabilitation of a conversion syndrome: a case report

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Context: The conversion syndrome is an uncommon finding in the general population, but it is frequently present in a hospital setting. It is often associated with certain populations and risk factors. The criteria for the diagnosis of a conversion syndrome are defined in international classifications. This disorder stimulates research in neurology and psychiatry. There is no standard treatment, which is therefore often adapted on case-by-case basis.

Questions: How should the therapist interact with the patient? How to structure the rehabilitation? What are the short- and long-term goals to achieve with the rehabilitation? How to prevent a relapse of conversion symptoms?

Methodology: Multidisciplinary clinical follow-up (including standardised scales) during eleven weeks of a young female patient who was treated in a neurorehabilitation centre for paraparesia and walking incapacity due to a conversion syndrome.

Results: Improvement of the paraparesia, recovery of walking capacity and activities of daily life. Remaining inability in professional reintegration.

Conclusion: The rehabilitation should be multidisciplinary. To encourage a reintegration of mind and body, we recommend defining successive short-term goals which will eventually help the patient to regain control over his or her symptoms.

P 26 Overall survival of methotrexate-treated patients with primary central nervous system lymphoma is associated with the variant transcobalamin 2 c.776C>G (p.P259R)

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Methotrexate (MTX) is an important anticancer drug and the most efficient chemotherapy component in primary central nervous system lymphoma (PCNSL). In a previous study we observed that the polymorphic missense variants transcobalamin 2 c.776C>G (p.P259R) and methylenetetrahydrofolate reductase c.1298A>C (p.E429A) were associated with the occurrence of confluent white-matter changes of the central nervous system in 65 PCNSL patients (Linnebank et al., Neurooncology, in press). In the present study we investigated whether these two variants of methionine metabolism were

associated with outcome. Overall survival of 55 patients who could be included in outcome analysis was 79 ± 7 months. The G-allele of the variant transcobalamin 2 c.776C>G was significantly associated with a shorter overall survival in Log Rank analysis, genotype CC (n = 16): 105 ± 7 months; CG (n = 23): 74 ± 11 months; GG (n = 16): 50 ± 10 months (Wald 5.6; p = 0.018; multivariate COX regression analysis). The other risk variant concerning white-matter changes, methylenetetrahydrofolate reductase c.1298A>C, was not significantly associated with overall survival, genotype AA (n = 27): 79 ± 11; AC (n = 22): 75 ± 11; CC (n = 6): 49 ± 10 (Wald 0.83; p = 0.363). These data suggest that the variant transcobalamin 2 c.776C>G (p.P259R), which has been suggested as risk factor for methotrexate side effects, also influences the therapeutic efficiency of methotrexate. Any effect of the variant methylenetetrahydrofolate reductase c.1298A>C might have been missed due to the low frequency of the C-allele. In contrast to an influence on methotrexate efficiency, the observed association may be due to an effect of the transcobalamin 2 variant on the natural course of PCNSL, which should be tested by analysis of a patient sample with a different treatment regimen. The data of this study, if confirmed in an independent patient sample, may provide novel ideas to improve the treatment of PCNSL and methotrexate-based therapies.

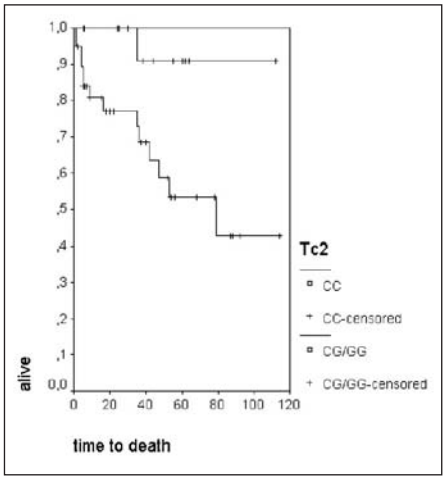

Figure: Kaplan-Meier curve of overall survival of the 55 PCNSL patients.

x = time to death in months; y = ratio of patients alive, censored cases are marked.

For graphical illustration only, the carriers of the CG and the GG genotype (lower survival line) were pooled and opposed to the carriers of the CC genotype (upper survival line).

P 27 Ping-pong gaze in a reversible post-ictal coma

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Periodic alternating or ping-pong gaze (PPG) is a slow and conjugated eye deviation from one side to the other with a fixed frequency and usually without pause.

We present clinical data and video of a patient presenting PPG in the setting of a post-ictal coma. This 59-year-old male suffered from severe traumatic brain injury with large left fronto-temporo-parietal and smaller right fronto-temporal hygroma causing mutism and right hemiplegia. Several months later, he was admitted to the emergency room after two generalised tonic-clonic seizures followed by coma secondary to urinary tract infection and tetraventricular hydrocephalus. After ventriculoperitoneal shunt, PPG disappeared. CT-scan showed decrease of ventricular enlargement and transependimar resorption and EEG non reactive diffuse theta/delta slowing that was more pronounced on the left frontal regions. With antibiotic and antiepileptic treatment, he gradually went back to his pre-existent state (mutism and right hemiplegia).

PPG is described in comatose patients predominantly with bilateral and extensive cortical lesions or more rarely with hypoxic/toxic encephalopathies, vermian or mesencephalic lesions. This case is another example of reversible PPG and the first in a post-ictal coma. Although its mechanisms are still debated, PPG is probably caused by a disconnexion of the cerebrum from horizontal gaze centres in the brainstem. Our case perfectly fits with this hypothesis.

P 28 Post-contrast FLAIR MRI demonstrates widespread blood-brain-barrier dysfunction in posterior reversible encephalopathy syndrome (PRES)

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Introduction: MR imaging in PRES may demonstrate typical patterns of vasogenic oedema. We describe a patient with peculiar brain MRI and CSF findings, supporting the pathophysiological theory of transient dysfunction of the blood-brain barrier (BBB).

Case report: A 49-year-old woman presented to the emergency room with nausea, severe headache, confusion, right pyramidal signs, cortical blindness and markedly elevated blood pressure (204/123 mm Hg). MRI findings indicated vasogenic oedema on T_2w- and ADC maps with slight cortical swelling. Post-contrast FLAIR showed widespread subarachnoid contrast collections mainly in the occipital and temporo-parietal regions. CSF analysis confirmed BBB dysfunction (massive protein elevation 2156 mg/l, albumin ratio of 40.8). PRES was treated and signs subsided over 24 h, follow-up MRI on day 6 and CSF follow-up were normal.

Discussion: This PRES case with typical CSF and MRI findings shows one new interesting feature: the subarachnoid hyperintensity on post-contrast FLAIR was indicative of BBB dysfunction and more widespread than the tissue changes. After contrast administration T_1 values in regions of BBB dysfunction are shortened from intravascular leakage of contrast medium into the extracellular space. Because the inversion time in FLAIR imaging is selected to null the CSF signal, a shortening of T_1 values due to contrast agent leakage results in incomplete suppression and marked hyperintensity. Post-contrast FLAIR is highly sensitive to demonstrate vascular leakage into the CSF space in a number of situations with BBB dysfunction and demonstrates PRES in more detail than conventional MRI.

P 29 Pramipexole and levodopa in the treatment of excessive daytime sleepiness in restless legs syndrome

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Background and objectives: The Swiss restless legs syndrome (RLS) study was conducted to compare efficacy and safety of the dopamine agonist pramipexole versus levodopa/benserazide in de novo patients with idiopathic restless legs syndrome. We here analyse data from this study in order to assess frequency and characteristics of excessive daytime sleepiness (EDS) and to evaluate the evolution of EDS under different RLS therapies.

Methods: Patients with idiopathic RLS, untreated, presenting symptoms almost daily, and with more than five periodic leg movements (PLM) per hour were included. The study was performed in five certified Swiss sleep-centres as a randomised, double-dummy, comparative crossover trial with two treatment periods of four weeks. For this study, we analysed data from 37 patients (21 women, 16 men).

Results: EDS, as determined by Epworth sleepiness scale (ESS) >10, was found in 32% of the patients. Sleepy RLS patients were younger ($p < 0.001$), no other differences between sleepy and non-sleepy RLS patients could be found. Pramipexole and levodopa were both effective in the treatment of RLS symptoms ($p < 0.001$ and $p = 0.002$). Pramipexole reduced excessive daytime sleepiness ($p = 0.05$).

Conclusions: In this RLS study excessive daytime sleepiness was commonly found. Both pramipexole and levodopa improve RLS symptoms. Only for pramipexole, there was a strong trend for reduction of EDS.

P 30 QEEG parameters as indicator for negative symptoms in patients with first-episode schizophrenia

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Background: While several studies showed an association of QEEG band power with negative symptoms in patients with schizophrenia, this has not been investigated in neuroleptic-naive first-episode patients (NNFE) up to now. We hypothesised delta (0.5–4 Hz) and theta (4–8 Hz) power to be augmented and alpha power to be diminished with increased negative symptoms in NNFE. We expected no relationship of positive symptoms and EEG band power.

Methods: We investigated 27 NNFE. Psychopathology was rated with Scale for the Assessment of Negative Symptoms (SANS) and the Brief Psychotic Rating Scale (BPRS). EEG was recorded from 8 electrodes with 10/20 system. After artefact removal a Fast Fourier Transform was performed across 7 frequency bands. Linear regressions with log-transformed power as dependent, psychopathology as independent and medication, drugs, age, sex, education, day time of EEG recording as confounding factors were calculated.

Results: A significant positive correlation of SANS with delta ($p = 0.04$) and theta ($p = 0.03$) could be replicated in NNFE. The negative correlation of alpha-power density with SANS scores could not be confirmed. Interestingly, we found beta1 (12–15 Hz) to be positively correlated with negative syndrome scale. As expected no relationship of BPRS summary score and EEG power could be found.

Conclusion: Former studies of QEEG in schizophrenic patients could be partially replicated in NNFE. Correlation of negative symptomatic with power of low-frequency bands could be confirmed. While reduction of power of alpha bands was observed in FE (Pflueger et al., 2008), there is no correlation with SANS. Recording EEG in beginning psychosis may be helpful in the diagnosis of a beginning negative syndrome in schizophrenia.

P 31 Reversible cortical blindness resulting from toxic levels of sirolimus

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A 26-year-old patient underwent allogenic human stem-cell transplantation due to a severe myelodysplastic syndrome in 2007. Immunosuppressive treatment consisted of methotrexate and cyclosporin.

One year after transplantation he was hospitalised with a slowly progressive primary demyelinating polyneuropathy including muscle weakness. Characteristic electrophysiological findings and a cytalbuminemic dissociation in CSF pointed towards a Guillan-Barré syndrome related to graft versus host disease. Plasmapheresis and subsequently intravenous immunoglobulins (IVIG) were administered. Neurotoxic effects of cyclosporine were suspected and consequently it was changed to sirolimus (3 mg twice daily). Clinical condition could be stabilised, however, no improvement was observed.

Toxic level of sirolimus (20.1 µg/l) was measured on day 17, sirolimus was paused for one day and then reduced to 1.5 mg twice daily.

On hospitalisation day 25, 13 and 8 days after discontinuation of plasmapheresis and IVIG respectively, the patient suddenly experienced complete visual loss of both eyes. Blood pressure was 135/79 mm Hg. On MRI imaging no diffusion abnormalities were apparent and no increase in T_2 hyperintense lesions could be demonstrated. Visual evoked potentials were absent, in contrast to the normal findings 12 days before. EEG revealed continuous bioccipital foci with occasionally epileptic discharges and no photic driving, whereas photic driving could be seen in pretransplantation EEG. Sirolimus blood level was 13.3 µg/l. Sirolimus was discontinued and intravenous magnesium treatment was initiated.

Visual symptoms improved within 3 days and vision came back to normal. Repeated visual evoked potentials were normal. Sirolimus blood level was 3.1 µg/l.

We suspect an episode of transient cortical blindness resulting from toxic levels of sirolimus. Cortical blindness in absence of structural lesions in the MRI may be resulting from an acute toxic cellular effect of sirolimus or of mild posterior reversible encephalopathy syndrome (PRES). PRES related to sirolimus has been reported recently [1, 2]. Thus, in immunosuppressed patients receiving sirolimus and presenting with acute cortical blindness, sirolimus could be the causative agent.

Literature

1 Bodkin CL, et al. Sirolimus-induced posterior reversible encephalopathy. Neurology. 2007;68:2039-40.
2 Moskowitz A, et al. PRES due to sirolimus. Bone Marrow Transplant. 2007;39:653–4.

P 32 S-adenosylmethionine in the cerebrospinal fluid is decreased in Alzheimer's disease: an effect of the apolipoprotein epsilon 4 allele?

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Increased plasma homocysteine levels have been described as an independent risk factor for Alzheimer dementia (AD), but the underlying pathophysiology has not yet been identified. This single-centre case-control study analysed different parameters of homocysteine metabolism in 60 AD patients and 60 control subjects: fasting plasma levels of vitamin B_{12}, folate and homocysteine as well as fasting cerebrospinal fluid (CSF) levels of folate derivates, of the methyl-group donor S-adenosylmethionine (SAM), of the SAM-degradation product and SAM-inhibitor S-adenosylhomocysteine (SAH) and of homocysteine. Additionally, the apolipoprotein E (APOE) genotype was determined.

As expected, the APOE4 allele was significantly overrepresented in AD patients compared with controls (0.27; Chi-square = 40.0; $p < 0.001$). In addition, AD patients had significantly lower CSF levels of SAM (193 ± 31 versus 207 ± 37; ANOVA; $F = 4.74$; $p = 0.032$) and significantly higher CSF levels of SAH (26.9 ± 6.2 versus 24.3 ± 6.8; $F = 4.44$; $p = 0.037$). Accordingly, also the SAM/SAH ratio, which represents the methylation capacity, was significantly lower in AD (7.6 ± 2.4 versus 9.1 ± 2.8; $F = 9.92$; $p = 0.003$).

Explorative analysis of all subjects showed that CSF SAM levels were significantly lower among carriers of the APOE4 allele (189 ± 30 nmol/L) compared with non-carriers (207 ± 36 nmol/L; $F = 6.93$; $p = 0.010$). Thus, the lower SAM levels in AD patients were at least partly explained by the APOE4 overrepresentation among the AD patients in comparison to the controls.

In summary, in our study sample SAM levels were significantly decreased in the CSF of AD patients. An association of the APOE4 genotype with SAM levels may be the underlying mechanism. If confirmed in an independent study sample, these results suggest a contribution of SAM decrease to the pathophysiology of AD. SAM substitution may be a candidate for the search of preventive and therapeutic strategies.

P 33 Sensibilité de l'examen neuropsychologique après ponction lombaire évacuatrice dans l'hydrocéphale à pression normale: une analyse rétrospective

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Introduction: L'hydrocéphalie à pression normale (HPN) est une anomalie neurologique définie par l'augmentation du volume des espaces contenant le liquide céphalo-rachidien et qui s'accompagne par des troubles de la marche et de l'équilibre ainsi que de signes de dysfonctionnement cognitif. La réalisation d'une ponction lombaire (PL) évacuatrice permet souvent une amélioration rapide et temporaire de la marche mais l'amélioration

du fonctionnement cognitif à 24 h n'est pas considérée fiable. Dans cette étude nous avons évalué l'utilité d'un examen cognitif post-PL différé (5 jours).

Méthodes: Nous avons analysé rétrospectivement 25 cas de suspicion d'HPN admis entre 2003 et 2005 dans la clinique de Neurologie de Genève. Les pathologies associées étaient une DTA dans 8/25 (32%), DFT 1/25 (4%), encéphalopathie vasculaire 7/25 (28%), HSA 1/25 (4%), troubles psychiatriques 2/25 (8%), Xfragile 1/25 (4%). L'évaluation spécifique comportait à l'admission: une analyse de la marche, une évaluation neuropsychologique et radiologique, et en post-PL (40 cc) une réévaluation de la marche et des modifications neuropsychologiques. Sur les 25 patients considérés, 23 ont bénéficié d'un re-test neuropsychologique à 5 jours post-PL. A la fin du bilan, ces 23 patients ont été classés soit HPN probable soit non probable en fonction de l'ensemble des éléments cliniques radiologiques et paracliniques.

Résultats: Sur les 25 patients analysés, 20 présentaient des troubles de la marche (80%), 12 des troubles sphinctériens (48%) et tous (25 patients) 100% des troubles cognitifs. Sur le plan cognitif, les épreuves le plus fréquemment altérées étaient le test d'apprentissage verbal (Buschke 16) dans 76% des cas et TMTb, Stroop et Hebb (52%) chacun. Le test cognitif le moins souvent déficitaire était la fluence grapho-phonémique avec 28%. Dans les 12 cas classés comme HPN probables, une amélioration neuropsychologique a été observée dans 7/12 cas (58%), alors que sur les 11 cas où le diagnostic de probabilité n'a pas été retenu, l'amélioration neuropsychologique a été retrouvée dans 2 cas (18%). La sensibilité et la spécificité des améliorations neuropsychologique post PL est respectivement 58 et 81%.

Conclusion: Dans notre collectif, l'évaluation neuropsychologique post-PL semble un test peu sensible mais relativement spécifique.

P 34 Sleep apnoea in multiple sclerosis fatigue

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Background and objectives: Fatigue is common in multiple sclerosis (MS) patients and has a major impact on health-related quality of life. Mechanisms and causes of fatigue are not well understood.

In 2–4% of the general population obstructive sleep apnoea syndrome is found, excessive daytime sleepiness and/or fatigue frequently occur in obstructive sleep apnoea. This study assessed frequency and characteristics of sleep-disorders breathing (SDB) in severely fatigued MS patients.

Methods: We studied 254 consecutive MS inpatients. Fatigue was measured with the Fatigue Severity Scale (FSS) and the Epworth sleepiness scale (ESS), severe fatigue was determined as FSS >4.5. Severely fatigued patients were studied using respiratory polygraphy.

Results: 112 (44%) out of 254 patients had an FSS score >4.5. 60 (54%) out of them were studied by respiratory polygraphy. Mean age was 49.1 years (range 21–75), there were 43 (72%) women and 17 (28%) men. Mean disease duration from first MS-symptom onset was 12.6 years (range 2–33 years), mean EDSS was 5.9. 49 (82%) patients had an Apnoea-Hypopnoea-Index (AHI) ≤10, in 5 (8%) patients AHI was >10 and ≤30, in 6 (10%) patients AHI was >30. Patients with AHI >30 had a mean BMI of 28.4, in comparison to 25.8 in the group of patients with AHI ≤10, mean EDSS was 6.3 (vs 5.6), there were 83% men (vs 20.4%). There was a significant correlation ($r = 0.56$; $p = 0.047$) between FSS and Beck Depression Inventory (BDI). No correlations between FSS, EDSS, duration of disease, Epworth sleepiness scale (ESS), body mass index (BMI), gender or age were found.

Conclusions: In our study in severely fatigued MS patients 18% suffered from SDB. SDB is frequent and, especially in obese male patients with an advanced disease progression, should be considered as a possible cause of fatigue. SDB was much higher in severely fatigued MS patients than in the normal population, therefore severely fatigued MS patients should undergo respiratory polygraphy. It needs to be evaluated whether SDB treatment (e.g. CPAP) can improve fatigue.

P 35 Sleep deprivation aggravates focal brain ischaemia in the rat

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Sleep-wake disturbances (SWDs) are frequently observed in stroke patients and are linked with poorer function outcome. Human and experimental data suggest a physiological role of sleep in neuronal recovery and neuroplasticity. The effect of sleep deprivation (SD) in the evolution after focal brain ischaemia is unknown.

Focal cerebral ischaemia was induced by coagulating the distal middle cerebral artery (MCA) in Spraque Dawley rats. 12 or 24 hours after induction of ischaemia, rats were subjected to 6 hours (n = 4 for both SD and control groups) or 12 hours (n = 6 for each group) of SD by gentle handling. Brain injury was evaluated by infarct volumetry and extension of neuronal death (as assessed by TUNEL staining).

6 h-SD (n = 4) had no effects ($p > 0.05$) neither on the infarct volume (SD 48.9 + 36.2 mm^3 vs 50.1 + 22.3 mm^3 in controls) nor on the number of tunnel-positive cells (SD 76.6 + 17.9 vs 73.1 + 19.8 in controls). In contrast, 12 h-SD significantly ($p < 0.02$) increased both infarct volume (SD 94.0 + 16.9 mm^3 vs 66.5 + 18.4 mm^3 in controls) and number of tunnel-positive cells (SD 1550 + 257 vs. 995 + 206 in controls). There was no significant ($p > 0.1$) increase in corticosterone level in the 12 h-SD group (213 + 99 ng/ml) when compared with the control group (137 + 63 ng/ml).

These results indicate that 12 h-SD aggravates brain injury in a rat model of focal cerebral ischaemia. Further studies are to investigate the involved mechanisms and functional consequences of these effects.

P 36 Spectral power density in the early course of schizophrenia

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Background: There is evidence for a drop in alpha2 and an excess in delta/theta power in patients with schizophrenia as compared with healthy controls (HC). This might be related to vulnerability or course of the disease. However, it is unclear whether this pattern of abnormal spectral power density is present already in the first episode (FE) or even in an at-risk mental state (ARMS) for psychosis.

Methods: EEG of 40 FE, 37 ARMS subjects and 24 HC were recorded under resting conditions with eyes closed. Fast Fourier Transform was performed. The power spectrum was subdivided into 7 bands. A Mixed Model Analysis was done with individuals as random factor, group and electrode as independent factors, and log-band power as dependent factor.

Results: There was a significant group main effect in the alpha2 ($F1; 62 = 5.29$; $p = 0.025$), theta ($F1; 62 = 9.61$; $p = 0.03$) and delta ($F1; 62 = 4.99$; $p = 0.029$) power density reflecting a higher power in HC than in FE patients. In general, power density in posterior parts of the brain was larger than in anterior parts as shown by significant Helmert contrasts according to mean power ordered electrodes. The inclusion of ARMS individuals diminished the overall group effect since the ARMS individuals' power almost perfectly fell into an intermediate range between FE and HC.

Conclusion: The classical pattern of spectral power in delta, theta and alpha2 has partially been replicated with alpha2-power decrease in FE. The findings in delta/theta power contradict earlier results. The additional consideration of ARMS subjects suggests that the observed pattern is stable and valid particularly in the prodromal state of schizophrenia. Therefore, we propose the alpha2/delta/theta-power density pattern to reflect a state-dependant alpha2 decrease while delta/theta increase might reflect chronicity.

P 37 Strong EBV-specific CD8+ T-cell response in patients with early multiple sclerosis

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Introduction: Epstein-Barr virus (EBV), in contrast to cytomegalovirus (CMV), has repeatedly been associated with a higher relative risk of developing multiple sclerosis (MS). Here, we studied the EBV- and CMV-specific T-cell responses in patients with MS, other neurological diseases (OND) as well as in healthy subjects (HC).

Methods: We enrolled patients with inflammatory MS, chronic MS, OND and HC and analysed the EBV- and CMV-specific T-cell responses by ELISPOT (IFN-gamma secretion).

Results: The EBV-specific CD4+ T-cell responses were similar between the groups, however, we found that EBV-specific CD8+ T cells in inflammatory MS patients secreted a higher amount of IFN-gamma than all other categories, including chronic MS patients. Interestingly, we found that the shorter the interval between MS onset and the assay, the higher the intensity of IFN-gamma secreting EBV-specific CD8+ T cells. However, the disease activity played no role as we did not find differences between MS patients in relapse or in remission.

By contrast, CMV-specific CD4+ T-cell responses were moderately enhanced in patients with inflammatory and chronic MS as compared to OND and HC subjects. No difference was found in the CMV-specific CD8+ T-cell responses and there was no correlation with the time elapsed since MS onset.

Conclusion: Our data suggest that EBV, more than CMV, might be involved in the onset of MS and that this effect might be mediated by CD8+ T cells.

P 38 Subclinical hyperthyroidism provoking seizure recurrence in idiopathic generalised epilepsy of the generalised tonic-clonic seizures (on awakening)-type

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Rationale: Subclinical hyperthyroidism (scHRT) has rarely been reported to be associated with seizure recurrence in idiopathic generalised epilepsy (IGE).

Methods: To report a patient with idiopathic generalised epilepsy (IGE) of the generalised tonic-clonic seizures (on awakening) (GTCS) type who experienced seizure recurrence when he had scHRT.

Results: The 20-year-old patient had Graves disease at age 15. After radioablation of the thyroid, he was substituted with oral L-thyroxine. He developed primarily generalised tonic-clonic seizures on awakening at age 17. Treatment with valproate was insufficient to control seizures and lamotrigine added. Side effects (tremor, weight gain) led to replacement of valproate by levetiracetam. Within stable periods he had two episodes with three breakthrough seizures. At both episodes antiepileptic drug (AED) levels were within therapeutic ranges and the EEG unchanged. However, lab results showed scHRT. Slight lowering of the daily intake of L-thyroxine led to normalisation of TSH levels and seizure freedom without changing the AED regimen.

Conclusion: Seizures provoked by thyroid hormone excess are a known phenomenon, but seizure recurrence resulting from scHRT has rarely been reported. It has been suggested that individuals with IGE seem to be particularly sensitive to changes in the thyroid hormone axis. Screening for scHRT in patients with IGE and otherwise unexplained breakthrough seizures might be appropriate.

P 39 Voxel-based morphometry – a method to study associations between regional grey-matter volume changes and white-matter lesions in the time course of multiple sclerosis?

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Background: Previous MR studies have established grey-matter (GM) abnormalities in MS with use of voxel-based morphometry (VBM). VBM will likely emerge as an important tool in understanding the topography, time course and clinical relevance of GM involvement in MS.

Objectives: Here we aimed at modifying voxel-based morphometry (VBM) to compare on a voxel-by-voxel basis GM volumes as measured by segmentation of conventional spin-echo MR images and white-matter (WM) lesions in order to assess the longitudinal trajectory of regional MRI changes. A major challenge for the use of VBM in MS studies, however, is the potential misclassification of WM lesions as GM.

Methods: In principle, we used a similar approach as in previous studies with some modifications: T_1-weighted three-dimensional MRI images and proton density images were acquired at baseline and one-year follow-up, preprocessed and analysed using statistical parametric mapping software (SPM5).

Preprocessing included the generation of 3D binary MS lesion masks by outlining the lesions on the proton density scans using a semi-automatic software in order to avoid misclassification of WM lesions as GM. SPM-processing included normalisation and segmentation, smoothing and parametric statistics. Segmentation accuracy was assessed by examining axial slices of each subject's GM, WM and CSF image in the individual's space. The warping accuracy was assessed by displaying axial slices from each subject with edges from the atlas image. Linear regression modelling (corrected for multiple comparisons at cluster level) was used for tissue-density comparison.

Results: Optimisation of VBM allowed us to detect longitudinal changes of GM volume in a number of regions with small structures such as the medial temporal lobes and the cingulate cortex. Additionally, an association of GM volumes with individual WM lesion volumes was shown.

Conclusions: Thus, VBM analysis of MS patients may serve as a suitable tool for the study of regional volume changes in MS-MRI images.

P 40 Effect of obstructive sleep apnoea in acute ischaemic stroke on blood pressure evolution and functional outcome

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Sleep apnoea (SA) and elevated blood pressure (BP) are frequent in acute stroke, but their association and impact on stroke outcome remain poorly investigated. Our aim is to explore (1) whether SA in the acute phase of stroke may affect long-term post-stroke BP evolution and (2) whether/to what extent both SA and elevated BP may affect functional stroke outcome.

We studied 42 consecutive patients with ischaemic stroke within 96 hours after onset. Stroke severity on admission and stroke outcome at discharge were assessed. Nocturnal breathing was recorded with a portable device the first night after admission. BP was measured with a portable device during the first 36 hours after admission. The same examinations were performed again at follow-up four months later.

Age was 61 ± 12. Both SA and BP significantly improved ($p < 0.0001$) at follow-up. The improvement of SA was entirely due to a decrease of central apnoeas, whereas obstructive apnoeas remained unchanged. Moderate-severe obstructive SA in the acute phase was associated with higher nocturnal BP levels in both the acute ($p = 0.008$) and recovery phase ($p = 0.005$) and with a worse functional outcome at follow-up ($p = 0.010$). The presence of ≥5 obstructive apnoeas/hour and/or of a nocturnal systolic BP ≥150 mm Hg in the acute phase were independent predictors of disability at follow-up (r2 of the full adjusted model 0.45).

SA and BP improve after stroke in most patients. Moderate-severe obstructive SA in the acute phase is associated with sustained higher post-stroke nocturnal BP levels, and both independently predict worse functional outcome.

P 41 Cerebrospinal fluid histamine levels are decreased in patients with narcolepsy and excessive daytime sleepiness of other origin

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Histaminergic neurons of the hypothalamic tubero-mammillary nucleus constitute a major wake-promoting system. In animals cerebrospinal fluid (CSF) histamine levels are increased after sleep deprivation and decreased during sleep. An involvement of the histamine system in human disorders has never been reported.

We measured by ultra high performance liquid chromatography/mass spectrometry histamine levels in lumbar CSF of 28 neurological patients with and without excessive daytime sleepiness (EDS) as assessed by the Epworth sleepiness scale (ESS). There were 10 patients with EDS (ESS >10, mean ESS = 14). Diagnosis included narcolepsy (n = 4), idiopathic hypersomnia (n = 2), sleep apnoea (n = 2) and multiple sclerosis (n = 2); their mean CSF histamine was 258 ± 159 pM. There were 18 patients without EDS (ESS <9, mean ESS = 5); their mean CSF histamine was significantly higher (629 ± 481 pM; p = 0.007). There was a significant inverse correlation (r = –0.48; p = 0.02) between ESS and both CSF histamine and hypocretin levels.

This study suggests that EDS is associated in humans with lower CSF histamine levels and therefore with a reduced activity of the wake-promoting histaminergic system.

P 42 Spezielle Entwicklungen der deutschsprachigen Neurologie im 18. und 19. Jahrhundert: Fortschritte abseits der Schulmedizin, Infrastruktur aus der Schule Johannes Müllers, Hauptrolle der Neuropsychiater

H. Isler

Zürich

1. Die Neurologie kam im 18. und frühen 19. Jahrhundert in freien medizinischen Schulen abseits vom Mainstream weiter voran.

2. Sie wurde im 19. Jahrhundert durch Johannes Müller und seine Schüler mit neuen Methoden der Grundlagenforschung aufgerüstet.

3. Von 1845 bis nach 1950 erschlossen Neuropsychiater die grundlegenden Strukturen und Funktionen des Nervensystems und entwickelten parallel dazu die Psychiatrie.

1. Auf Nebengeleisen: Animismus, Vitalismus, Phrenologie, Mesmerismus

Diese freien Schulen suchten nach Interaktionen zwischen Körper und Seele. Sie waren für die Entwicklung der Neurologie besser geeignet als die Schulmedizin, die psychische und physische Sachverhalte trennte. Stahls animistische Schule in Halle förderte schon 1746 die Elektrotherapie, und seine vitalistischen Nachfolger Sauvages und Prochaska postulierten vor Galvani die elektrische Nervenleitung, die Haller noch strikte ausschloss. Gall, der Gründer der Phrenologie, versuchte, Hirnorgane anatomisch nachzuweisen, was ihm misslang. Er wurde zum führenden Hirnanatomen seiner Zeit und beschrieb die Pyramidenbahn. Seine Themen wirkten weiter. Reil, Haupt der Vitalisten, erfand den Begriff «Psychiatrie», empfahl Psychotherapie, forderte psychiatrische Kliniken, verbesserte die Konservierung der Hirnpräparate und definierte die Insula Reili und andere noch nicht bekannte Hirnteile. Schliesslich fand der Mesmerist Kerner das Botulinumtoxin und testete es am eigenen Leibe.

2. Johannes Müller und seine Schüler entwickeln die Grundlagenforschung

Johannes Müller in Berlin war Vitalist und integrierte die Psychologie in sein Handbuch der Physiologie. Seine Schüler aber wurden meist Mechanisten. Du Bois Reymond schuf die moderne Elektrophysiologie; Helmholtz erforschte das Gehör, mass die Nervenleitung und erfand den Augenspiegel; Schleiden, Schwann und Remak entdeckten die Pflanzen-, Tier- und Nervenzellen; Virchow machte daraus seine Zellularpathologie und beschrieb die Glia; Kölliker begründete die moderne Histologie; Brücke und Ludwig entwickelten die mechanistische Physiologie; und Wundt, Ex-Laborchef von Helmholtz, entwickelte die experimentelle Psychologie.

3. Die Neuropsychiater teilen das Gehirn und die Psychiatrie ein

Griesinger begründete 1845 die deutsche Neuropsychiatrie und danach die Klinik Burghölzli, die mit Gudden, Hitzig, Forel, Bleuler, Adolf Meyer und Oskar Vogt für Psychiatrie und Neurologie wegweisend wurde. Motorik, Somatosensorik, Hören und Sehen ordneten deutschsprachige Neuropsychiater seit Meynert den Frontal-, Parietal-, Temporal- und Occipitallappen zu. Türck, Meynert, Gudden, Forel, Munk und Monakow lokalisierten die Hauptfunktionen des Gehirns anhand der sekundären Degeneration, Flechsig anhand der embryonalen und kindlichen Entwicklung des Nervensystems, und Fritsch und Hitzig mit der Elektrostimulation an Hunden. Möbius prägte die Begriffe endogen und exogen, Kraepelin, Bonhoeffer und Bleuler bauten sie in ihre Psychiatrie ein. Der frühere Hypnotiseur Vogt gründete vier interdisziplinäre Hirnforschungsinstitute, deren Forschungsansätze bis heute weiter geführt werden. Die Breslauer Wernicke und Foerster prägten die klinische Neurologie des 20. Jahrhunderts. Der Niederweninger Neuropathologe Adolf Meyer reformierte die amerikanische Psychiatrie. Die interdisziplinären Modelle von Foerster und den Vogts führten zu den grossen Handbüchern der klinischen Neurologie, zur modernen Paraplegie-Rehabilitation, zum polygraphischen EEG und zu den klinisch-physiologischen Neurologieabteilungen von und nach Jung. Noch um 1955 fand der Neuropsychiater Roland Kuhn die trizyklischen Antidepressiva.

Diese Entwicklungen zeigen, dass Forscher, die Psyche und Verhalten in ihre physischen Untersuchungen mit einbezogen, die Funktionen des Nervensystems soweit überblickten, dass sie ihre Untersuchungen gezielt ansetzen, neue Methoden integrieren und die Ergebnisse sinnvoll einordnen konnten. Deshalb fanden deutschsprachige Neuropsychiater die regionalen Funktionen des Hirns.

P 43 Brains of young spontaneously hypertensive rats show abnormal neurovascular units that may cause cerebrovascular diseases

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Subcortical arteriosclerotic leukoencephalopathy is a distinct form of cerebral angiopathy resulting in functional and intellectual impairments (vascular dementia). Hypertension is a main risk factor for developing this cerebrovascular disease. The molecular mechanisms involved in the progression of the disease are not yet known. To find early cerebral abnormalities that may induce the disease, we analysed the brains of the Spontaneously Hypertensive Rats (SHR), sharing several similarities with essential hypertension in humans and are therefore considered a good experimental model.

Brain tissue sections of SHR and normotensive Wistar Kyoto rats (WKY) aged 2, 4, 6 and 9 months were used to study the density of small vessels and astrocytes, the two major components of the neurovascular unit, in the cortex and striatum using immunofluorescent staining. In order to explain the difference in the vessel densities between both strains, the expression pattern of VEGF (vascular endothelial growth factor), an important factor involved in angiogenesis, was analysed. Furthermore, the hypoxic status of the brain was studied in both strains by detecting the accumulation of HIF-1a.

SHR showed a higher density of col4-positive vessels in the cortex and in the striatum than WKY, with significant differences in 2-month- (pre-hypertensive) and 4-month-old (hypertensive) rats. Preliminary results from 2-month-old animals further showed a higher proportion of VEGF-positive vessels in young SHR than in WKY in the cortex and putamen. SHR showed less astrocytes than WKY, but astrogliosis at 9 months in the cortex. Hypoxia was observed in SHR only, at the age of 9 months, as revealed by the accumulation of HIF-1a in neurons of the cortex and putamen.

Pre-hypertensive and young hypertensive SHR show a higher small-vessel density in their brains. The higher proportion of VEGF-expressing vessels observed in pre-hypertensive rats may indicate that angiogenesis is induced in this strain before hypertension occurs. These animals possess less astrocytes, indicating that the neurovascular unit may not be normal, and they show signs of hypoxia at 9 months of age. These results suggest that early neurovascular dysfunction in young individuals may induce ischaemic infarcts later in life.

P 44 Entwicklung der Neurologie im 17. Jahrhundert an der Universität Oxford

H. Isler

Zürich

In der Mitte des 17. Jahrhunderts trafen in Oxford einige Neuerungen zusammen, die die Entwicklung der Neurologie begünstigten. Eine materielle Seele wurde Tieren und Menschen zugeschrieben, deren Funktionen durch die Anatomie des Nervensystems und durch Tierversuche erforscht werden konnten. Induktive Methoden wurden durch den Begründer der englischen Biochemie und Epidemiologie, Thomas Willis, verwendet und beschrieben (1659). Die Experimentierfreude der Vertuosi, aus denen die Royal Society entstand, führte zur Forschung als Teamwork, von Willis als Leiter seines Chemielabors eingeübt. 1658 hatte J. J. Wepfer in seinem Buch über Schlaganfälle (zitiert von Willis) die Farbstoffinjektionen der Hirngefässe bei Sektionen eingeführt.

William Petty hatte in Leiden die Neuroanatomie des Franciscus Sylvius beim Sezieren erlernt und brachte sein Knowhow um 1650 Willis bei, indem er mit ihm Gehirne sezierte und vergleichende Neuroanatomie betrieb. Willis setzte diese Untersuchungen mit einem Team hochqualifizierter Kollegen fort und publizierte 1664 seine *Cerebri Anatome,* die erste Monographie über Neuroanatomie, die im gleichen Jahr in vier verschiedenen Ausgaben in England und Holland erschien und bis 1720 nachgedruckt wurde. Darin prägte er das Wort «Neurologia» und versprach, seine «Psychologia» folgen zu lassen, die er dann in «De Anima Brutorum» 1672 vorstellte: die Lehre von der materiellen Seele der Tiere und Menschen als Gesamtheit der Funktionen des Nervensystems. Das Buch hat einen physiologischen und einen pathologischen Teil, besteht also aus einem Lehrbuch der Neurophysiologie und einem Kompendium neuropsychiatrischer Syndrome, mit frühen Beschreibungen der Myasthenie, der Restless legs, der Narkolepsie und der progressiven Paralyse.

1667 hatte er auch ein Buch über Krampfkrankheiten publiziert, in dem er die Blut-Hirn-Schranke und die Parkinson-Krankheit beschrieb. So hat Willis mit seinen Teams die systematische Hirnforschung und die Neurologie als Disziplin entwickelt und wesentliche Themen der Neurologie erkannt und vorgestellt.

P 45 Development of ICF core sets for multiple sclerosis

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Background: With the approval of the WHO's International Classification of Functioning, Disability and Health (ICF) there is now a universally accepted framework to classify and describe functioning, disability and health in individuals with health conditions. The ICF is a very comprehensive classification with 1454 so-called ICF categories. For its application in clinical practice tools, such as ICF Core Sets, are needed. ICF Core Sets are agreed-on lists of ICF categories relevant for the description of functioning of individuals with a specific health condition.

Objectives: The objective of the project was the development of ICF Core Sets for Multiple Sclerosis (MS) to specify functioning and disability of individuals with MS.

Methods: The ICF Core Sets for MS were decided during an international consensus conference. Twenty-one experts from all over the world and from different health professions (physicians, nurses, physiotherapists, occupational therapists, speech and language therapists, psychologists, social workers) took part in this conference. The participants of the conference decided on the ICF Core Sets for MS according to a multistage and established decision process which integrates evidence from four preparatory studies: (a) cross-sectional empirical study, (b) systematic literature review, (c) expert survey including health professionals and (d) qualitative study using focus groups (see fig. 1).

Results: The ICF categories that constitute the ICF Core Sets for MS were identified in an iterative decision-making and consensus process with discussions and voting. Since the requirements to describe functioning in MS are different for a comprehensive multidisciplinary clinical assessment and a research setting, Comprehensive and Brief ICF Core Sets for MS were developed. The Comprehensive ICF Core Set for MS includes 138 ICF categories to describe the prototypical spectrum of limitations of functioning in a multidisciplinary assessment. Instead, the Brief ICF Core Set for MS includes 37 candidate ICF categories to describe the prototypical spectrum of limitations of functioning in clinical studies.

Conclusions: With the ICF Core Sets for MS we can now rely on an international standard of ICF categories to be relevant in patients with MS to specify functioning. It is expected that the ICF Core Sets for MS will profoundly influence the treatment and rehabilitation of MS patients, clinical practice and research studies.

The project is being funded by Hertie Foundation.

P 46 Prediction of discharge destination after neurological rehabilitation in stroke patients. Significance of functional abilities, cognition and age

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Background: Return home is the most important goal of stroke patients admitted to rehabilitation. We aimed to identify predictive variables for the outcome "return home after rehabilitation" in a large cohort of stroke patients.

Patients and methods: Analysis of a single-centre neuro-rehabilitation database covering all patients admitted for stroke (ischaemic or haemorrhagic) between 1996 and 2007. We excluded patients with a length of stay

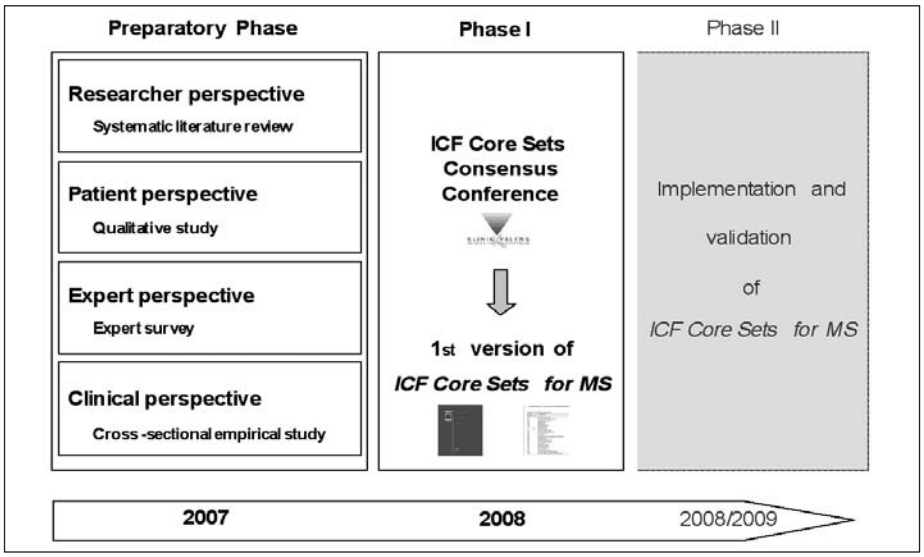

Figure 1
Development of ICF Core Sets for multiple sclerosis.

(LOS) in rehabilitation <5 days (n = 8). The following baseline parameters were routinely recorded: age, sex, living alone or with another person, need of professional help before stroke onset in activities of daily living, prior stroke, presence of hypertension, diabetes, tobacco use, atrial fibrillation, carotid stenosis, presence of a gastrostomy (PEG) or urinary catheter and LOS in acute care. Stroke syndrome was classified according to OCSP classification [1], aetiology according to TOAST criteria [2]. On admission, a routine neurologic examination was performed and the presence of aphasia, dysarthrophonia, hemineglect, hemianopia, trunk control while sitting or standing and walking ability (10 m unassisted with or without walking aid) was recorded.

Within 72 hours from admission, basic activities of daily living (BADL) were assessed by the interdisciplinary team with the Functional Independence Measure (FIM [3]). FIM is an 18-item assessment tool with a 7-point ordinal scale for each item and two main subscores (motor and cognitive) as well as 6 minor subscores (self-care, continence, transfers, locomotion, communication and social cognition). FIM scorings were made by consensus in the interdisciplinary team.

For analysis discharge destination was dichotomised into return home and all other discharge destinations, comprising death, nursing home and readmission to acute care. Multiple logistic regression was used to create predictive models. The accuracy of the models in predicting "return home after rehabilitation" was assessed by receiver operating characteristic (ROC)-curves using the predicted probabilities of the logistic regression.

Data analysis was performed with SPSS package 12.0.

Results: 1332 patients were included. Baseline parameters are outlined in table 1. Age-distribution was similar to an epidemiologic study of stroke in the Canton Basel-Stadt in 2002 (fig. 1) [4]. 62.4% of patients returned home after rehabilitation, 2.7% died during rehabilitation, 23.9% went to a nursing home and 10.9% had other discharge destinations.

In univariate analysis, return home was significantly correlated to gender, living with partner, atrial fibrillation, need of professional help before stroke, aphasia, hemianopia, FIM total score and all subscores, presence of urinary catheter or PEG, trunk control while sitting and standing and walking ability.

In multiple logistic regression living with partner, trunk control while sitting, motor and social-cognitive FIM subscores and age remained independent predictors (table 2). The area under the curve (AUC) of the final model was 0.86 (95% confidence interval [CI] 0.84–0.88). When age was excluded from the model, the AUC virtually remained the same (AUC 0.85, 95% CI 0.83 – 0.87) (fig. 2).

Conclusion: Return home after stroke rehabilitation in our cohort is determined by functional abilities in motor and social-cognitive domains and presence of a living partner. Trunk control while sitting at the beginning of rehabilitation is an additional favourable predictor. Age, though also independently associated with discharge destination, adds little to the predictive power of these variables.

Poster SGPP

P 47 Altersveränderungen bei komplexen Sprachleistungen

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Hintergrund: Im normalen Alterungsprozess kommt es zu einer Vielzahl von anatomischen und funktionellen Veränderungen. Von diesem Prozess sind unter anderem viele unterschiedliche kognitive Systeme betroffen. Welchen Veränderungen jedoch höhere sprachliche Leistungen im normalen Alter unterliegen, ist bis heute nur bedingt geklärt.

Fragestellung: Ziel der vorliegenden Arbeit war die Erfassung von komplexen sprachlichen Funktionen bei gesunden Menschen ab einem Alter von 20 Jahren unter spezieller Berücksichtigung des Bildungsniveaus. Folgende Sprachbereiche wurden überprüft: Benennen nach Definition, Synonyme, Antonyme, Kohärenzentscheiden und Bildung von Sätzen.

Methoden: Es wurden insgesamt 100 Probanden getestet, davon konnten 91 Datensätze (46 Männer, 45 Frauen) zu einer weiteren statistischen Analyse genutzt werden. 9 Personen mussten wegen Nichterfüllung der vorher festgelegten Einschlusskriterien von der Auswertung ausgeschlossen werden. Bildungsniveau und Alter wurden jeweils in drei vergleichbare Gruppen unterteilt: «bis 10 Bildungsjahre», «11–13 Bildungsjahre» und «14 Bildungsjahre und mehr» bzw. «bis 39 Jahre», «40–59 Jahre» und «60 Jahre und mehr». Im Mittel waren die Personen 50 Jahre alt (Minimum 21 Jahre, Maximum 82 Jahre) und wiesen im Schnitt 12 Jahre institutioneller Bildung (Minimum 8, Maximum 20) auf.

Ergebnisse: Unter Anwendung nichtparametrischer statistischer Analyseverfahren (Mann-Whitney U-Test, Kruskal-Wallis-Test) zeigten sich beim Test Antonyme signifikante Unterschiede sowohl in bezug auf das Alter ($p = 0{,}044$) als auch auf die Bildung ($p < 0{,}001$). Die Tests Benennen nach Definition ($p = 0{,}005$) und Sätze bilden ($p < 0{,}001$) zeigten hingegen ausschliesslich eine Differenzierung hinsichtlich des Alters. Die Tests Synonyme und Kohärenzentscheiden blieben hingegen unempfindlich gegenüber einer alters- und bildungsabhängigen Veränderung.

Schlussfolgerung: Die Anwendung dieser Testverfahren, bzw. Überprüfung von höheren Sprachleistungen bei Patienten mit neurologischen Erkrankungen, im speziellen der Einfluss des Alters und der Schulbildung auf die Ergebnisse, könnte Ausgangspunkt für weitere Untersuchungen sein, vor allem könnten jene Testverfahren eine Rolle spielen, die im Rahmen dieser Untersuchung keine alters- und bildungsabhängigen Effekte zeigten.

P 48 Physical pain in patients with depressive symptoms in Switzerland: a field report from clinical practice

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The present study is a cross-sectional observation of 586 patients suffering from chronic pain and depressive symptoms from all over Switzerland who were treated with Venlafaxin in 122 medical practices. Pre-existing or other additional, anti-depressant medication was not taken into account. Diagnosis of depression was determined by a regular clinical interview, pain intensity was estimated using a visual analogue scale (VAS), and severity of disease was rated by the Clinical Global Impression scale (CGI). Age, gender, duration of depression and all clinically approved diagnoses for comorbid somatic and mental disorders (i.e. the first digit according to ICD-10) were listed. The use of opioid and non-opioid analgesics and the number of therapies in addition to those targeting depression and pain were also recorded. Compared with Central European patients, those from the Balkans and Southern Europe appear to present with more intense, overall pain mainly affecting the head, extremities and back, whereas Southern Europeans tend to suffer even more frequently from chest pain compared with their Central European peers. Furthermore, the study suggests that, compared with primary care providers, psychiatrists are treating considerably younger, more severely sick patients from the Balkans presenting with essentially head pain of greater intensity.

P 49 Physician speciality and pain reduction in patients with depressive symptoms under treatment with venlafaxine

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Excessive pain perception may lead to unnecessary diagnostic testing or invasive procedures to result in iatrogenic complications and prolonged disability. Naturalistic studies on depressed patients with chronic pain investigating the impact of medical speciality on treatment outcome in a primary care setting are lacking. Venlafaxine and other antidepressants may alleviate pain in depressed patients. In this observational

study, we examined whether the magnitude of pain reduction in 444 depressed patients under venlafaxine would differently relate to the medical speciality of the 122 treating physicians, namely psychiatrists (n = 110 patients), general practitioners (n = 236 patients) and internists (n = 98 patients). Independent of demographic factors, comorbidity, severity of pain and illness at study entry, and the duration of pain and depression, patients seemed to profit significantly less in terms of pain reduction ($p < 0.001$) and of reduction in severity of their illness by psychiatrists as compared to general practitioners ($p < 0.019$) and internists ($p < 0.002$). The findings suggest that patients referred to psychiatrists are more difficult to treat than those referred to general practitioners and internists. Therefore, psychiatrists could particularly profit from educational programs targeting at improving their capacities in treating pain of their depressed patients.

P 50 Regional origin and decrease of pain in patients with depressive symptoms under treatment with venlafaxine

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Background: Worldwide data are extensively lacking in regard to the effect of regional origin on decrease of pain in patients with depressive symptoms under therapy with antidepressants in the primary care setting.

Objective: We conducted a prospective naturalistic observational trial on 420 pain sufferers with depressive symptoms from all over Switzerland who were treated with venlafaxine by 122 physicians in primary care.

Methods: We hypothesised that the magnitude of pain reduction under treatment with venlafaxine differently relates to regional origin of patients. Previous and additional antidepressant medication was not taken into account. Physicians rated illness severity using the Clinical Global Impression severity scale and pain intensity by means of visual analogue scales.

Results: Compared with Middle European patients (ME), those from Eastern Europe (EE) and Southern Europe (SE) were younger and presented more intense overall pain mainly affecting the head, extremities and back. In addition, SE patients suffered more intense thoracic pain than ME patients, and EE patients suffered less frequently from abdominal pain compared to their ME and SE counterparts. Furthermore, 3 months after study entry, ME patients were found to profit more from treatment with venlafaxine in terms of overall illness severity and pain intensity than patients from EE and SE.

Conclusion: Regional origin may contribute to the magnitude of pain reduction in patients with depressive symptoms under treatment with venlafaxine. Our results provide a rationale for care-provider educational programs aimed at improving capacities in treating patients from different regional origin with psychosomatic complaints such as depression and comorbid pain.

P 51 Study on sex differences in interpersonal problems of alcohol-dependent patients and controls: preliminary results

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Introduction: There is no specific addictive personality but alcoholism is associated with specific personality traits, which may lead to certain interpersonal problems in alcohol-dependent patients.

Methods: In this ongoing study 60 alcohol-dependent patients have been recruited after detoxification. Three questionnaires were administered: patients' interpersonal problems were measured with the Inventory of Interpersonal Problems (IIP-64) which was also applied to 60 healthy controls. Additionally, alcohol-dependent patients were interviewed with the Alcohol Use Disorders Identification Test (AUDIT) to assess the severity of alcohol dependence. Finally, patients were subtyped according to Lesch's typology.

Results: Preliminary results suggest that interpersonal problems of alcohol-dependent men do not differ from healthy male controls. Women with alcohol dependence rated themselves as significantly more self-sacrificing than female controls. The most frequent Lesch type in this sample was type 3 (50%), followed by type 2 (24%), type 4 (20%) and type 1 (6%). Comparing interpersonal problems of Lesch's typology, there was a trend that type-2 patients (conflict drinking type) rated themselves as significantly less non-assertive and less overly accommodating than type-3 patients (depressive drinking type).

P 52 Zürcher Stufenplanstudie: Algorithmusgestützte Depressionsbehandlung und Symptomremission bei stationären Patienten

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Einleitung: Depressive Erkrankungen gehören zu den bedeutendsten Krankheitsbildern des zentralen Nervensystems. Trotz des verbesserten psychotherapeutischen und pharmakologischen Behandlungsangebotes sprechen 30–50% der Patienten nur teilweise auf die Behandlung an, bis zu 20% der Fälle nehmen einen chronischen Verlauf. Als eine der Hauptursachen wird ein unzureichend koordinierter Einsatz der verbesserten Therapiemöglichkeiten, d.h. eine inadäquate und unstrukturierte Therapie angesehen. Strukturierte Therapiealgorithmen gelten mittlerweile als geeignete Instrumente zur Optimierung der antidepressiven Therapie und sollen im Rahmen der Zürcher Stufenplanstudie evaluiert werden.

Methode: Ein Patientenkollektiv (N = 100, Alter 18–80 Jahre), das an einer leichten bis schweren Depression mit oder ohne psychotischen Symptome (ICD-10-Kriterien) leidet, wird in einem maximal 18wöchigen Behandlungsprotokoll zufällig der SSTR (standardised stepwise drug treatment regimen)- oder TAU (treatment as usual)-Gruppe zugewiesen. Als primäres Messinstrument wird die Hamilton-Depressions-Skala (HAMD-21) verwendet. Ein Wert von 8 gilt als Remission. Bei Partialremission oder Therapiemisserfolg wird nach der anfänglichen 6wöchigen Antidepressiva-Monotherapie die Behandlung gemäss Algorithmus fortgeführt.

Diskussion/Ergebnisse: Durch die Einführung eines systematischen Behandlungsalgorithmus kann die Therapieresistenz und/oder mangelndes Ansprechen auf Therapie vermieden und die Behandlungsqualität gesteigert werden. Der Nutzen systematischer Therapiealgorithmen soll in bezug auf das Therapieergebnis, die Qualität der Behandlung, die Patientenzufriedenheit sowie gesundheitsökonomische Parameter überprüft werden. Es werden die ersten Ergebnisse präsentiert.

P 53 Zürcher Stufenplanstudie: Erhebung neuropsychologischer Defizite bei stationären depressiven Patienten im Verlauf

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Einleitung: Neuropsychologische Beeinträchtigungen sind ein wesentliches Merkmal depressiver Erkrankungen. Die Reversibilität kognitiver Beeinträchtigungen ist trotz Besserung der depressiven Symptomatik oft unvollständig. Nur wenige Befunde liegen zur Frage vor, ob diese kognitiven Defizite im remittierten Zustand persistieren. Wir gehen im Rahmen des grösseren Gesamtprojektes

der Zürcher Stufenplanstudie dieser Fragestellung nach.

Methode: In einem längsschnittlichen Design werden kurz nach der stationären Aufnahme in die Psychiatrische Klinik, nach sechs Wochen sowie sechs Monaten nach der Entlassung umfangreiche neuropsychologische Untersuchungen durchgeführt, welche die Bereiche Gedächtnis, Aufmerksamkeit und exekutive Funktionen beinhalten. Folgende neuropsychologischen Tests wurden an bisher 28 unipolar depressiven Patienten angewendet: Alertness, selektive und geteilte Aufmerksamkeit aus der Testbatterie zur Aufmerksamkeitsprüfung (TAP 2.1), Rey-Oesterrieth Complex Figure Test (RCFT), Verbaler Lern- und Merkfähigkeitstest (VLMT), Trail Making Test A und B, Aufmerksamkeits-Belastungs-Test (Test d2), Zahlen- und Blockspanne vorwärts bzw. rückwärts aus dem Wechsler Gedächtnistest (WMS-R), Regensburger-Wortflüssigkeits-Test (RWT). Der Mehrfachwahl-Wortschatz-Intelligenztest (MWT-B) diente der intellektuellen Leistungserfassung. Als Normierung wurden die neuropsychologischen Tests mit 20 gesunden Kontrollpersonen durchgeführt.

Diskussion/Ergebnisse: Das kognitive Leistungsniveau nach sechs Wochen bzw. sechs Monaten wird mit demjenigen vom Untersuchungsbeginn verglichen und mit der Symptombelastung in Zusammenhang gebracht. Das Ziel ist eine detaillierte Charakterisierung kognitiver Beeinträchtigungen und deren Bedeutung für den weiteren Verlauf der Erkrankung. Ebenfalls wird das Ausmass neuropsychologischer Defizite in beiden randomisierten Gruppen der Zürcher Stufenplanstudie, des strukturierten Therapiealgorithmus (standardised stepwise drug treatment regimen, SSTR) und der Kontrollgruppe (treatment as usual, TAU), miteinander verglichen. Die Ergebnisse sollen die umfassende kognitive Beeinträchtigung verdeutlichen, die unabhängig von der Remission der Depression weiter bestehen können und sollen die Relevanz kognitiver Rehabilitationsmassnahmen hervorheben. Konsequenzen im Hinblick auf Therapieresistenz, Rezidive und soziale Integration sollten eingehend untersucht werden.

P 54 Zürcher Stufenplanstudie: unterschiedliche Behandlungsergebnisse bei stationären Patienten mit einer ängstlichen vs. nicht-ängstlichen Depression

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Einleitung: Bei etwa der Hälfte aller Patienten mit einer depressiven Erkrankung wird ebenfalls ein klinisch signifikantes Angstniveau festgestellt. Depressionen mit Angstsymptomen haben vermutlich eine ungünstige prognostische Bedeutung.

Methode: Aus dem Patientenkollektiv des grösseren Gesamtprojekts der Zürcher Stufenplanstudie (N = 100, Alter 18–80 Jahre), das an einer leichten bis schweren Depression mit oder ohne psychotische Symptome (ICD-10-Kriterien) leidet, werden zwei Gruppen gebildet: ängstlich-depressive Patienten mit einem Punktwert von 7 bei Aufnahme gemessen anhand des Angst-/Somatisierungsfaktors der Hamilton-Depressions-Skala (HAMD-21) und Patienten mit einer nicht-ängstlichen Depression. Schwere der depressiven Symptomatik, kognitive Leistungsfähigkeit, soziale Situation und Lebenszufriedenheit werden mit standardisierten Instrumenten erfasst. Sowohl die Remissions-/Responseraten als auch die Behandlungsdauer werden bei Patienten mit und ohne Angst verglichen und ausgewertet.

Diskussion: Es besteht die Annahme, dass aus dem Anteil von ängstlich-depressiven Patienten signifikant weniger remittieren und die Remissionszeit verzögert ist. Im Vergleich zu den anderen depressiven Patienten sollen die ängstlichen Patienten häufiger kognitiv beeinträchtigt und unzufriedener damit sein, wie andere Personen mit ihrer Erkrankung umgehen. Darüber hinaus werden Häufigkeit und Intensität der Nebenwirkungen sowie die Symptombelastung erhoben und das Ansprechen auf Medikamentenwechsel- und/oder -aufdosierung in beiden randomisierten Gruppen der Zürcher Stufenplanstudie, des strukturierten Therapiealgorithmus (standardised stepwise drug treatment regimen, SSTR) und der Kontrollgruppe (treatment as usual, TAU), miteinander verglichen.

P 55 Alkoholabhängigkeit und TMS-Doppelpulsmethode (dpTMS)

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Hintergrund/Fragestellung: Mit Hilfe der dpTMS ist es möglich, sowohl inhibitorisch (verlängerte Reaktionszeit) wirkende als auch fazilitatorische (bahnende Voraktivierung) Prozesse im motorischen System getrennt zu erfassen. Bei alkoholabhängigen Patienten wird in verschiedenen neuronalen Netzwerken, so auch im motorischen System, eine Änderung der inhibitorischen und fazilitatorischen Kontrolle diskutiert.

Methoden: Für diese Studie wurden insgesamt 21 Männer (alle Rechtshänder) im Alter zwischen 18 und 65 Jahren untersucht, die sich aus 10 alkoholabhängigen und 11 gesunden Probanden zusammensetzten. Die Gruppe der Alkoholpatienten wurde vor Beginn des Entzugs (Baseline), nach 3 Wochen und nach 7 Wochen mittels dpTMS getestet. Die Kontrollgruppe wurde zu zwei Zeitpunkten (Baseline und nach 3 Wochen) untersucht. Bei jeder Testung erfolgte vorab die Bestimmung der individuellen motorischen Reizschwelle und anschliessend eine Stimulationssession im Umfang von 80 randomisierten Trials (Stimuli mit Interstimulusintervall [ISI] von 2, 3, 5, 10 und 15 ms, jeweils 10 Trials; 10 Trials ohne Stimulus und 20 Einzelstimuli) im Abstand von jeweils 200 ms. Statistische Auswertung mittels ANOVA.

Ergebnisse: In der Baseline zeigten Alkoholpatienten zum ersten Messzeitpunkt signifikant höhere Werte bei den inhibitorischen ISIs von 2 ms ($p < 0.001$) und 3 ms ($p < 0.001$) und eine signifikant niedrigere MEP-Amplitude bei den fazilitatorischen ISIs von 10 ms ($p < 0.008$) und 15 ms ($p < 0.005$) im Vergleich zu den Kontrollen. Nach drei Wochen ergaben sich noch statistisch relevante Unterschiede bei den inhibitorischen ISIs von 2 ms ($p < 0.001$) und 3 ms ($p = 0.01$), beim dritten Messzeitpunkt unterschieden sich die beiden Gruppen lediglich beim ISI von 2 ms ($p = 0.003$). Bei einem ISI von 5 ms unterschieden sich die Gruppen zu keinem Messzeitpunkt.

Schlussfolgerungen: Die Untersuchung unterstützt die Hypothese, dass sich im Laufe des Alkoholentzugs die kortikale Erregbarkeit und damit kurzfristig die Neuroplastizität des motorischen Kortex verändert. Aus Grundlagenuntersuchungen zum TMS lässt sich dieser Verlauf am ehesten auf eine Reduktion bzw. Modifizierung Glutamatabhängiger Projektionen zurückführen, die wiederum eine erhöhte Empfindlichkeit des zentralen dopaminergen Systems verursachen, welches bei einer Alkoholabhängigkeit bzw. -entzug eine wesentliche Rolle spielt. Die veränderte kortikale Inhibition bei Alkoholabhängigkeit könnte somit einen biologischen Marker darstellen, der Veränderungen im glutamatergen System messbar macht.

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P 56 Hypoperfusion and reduced fMRI activation of the fusiform face area in patients with delusional misidentification syndrome

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The fusiform face area (FFA), located within the right fusiform gyrus, is critical for human face processing. In schizophrenia patients face processing was shown to be impaired, along with a volume reduction of the fusiform gyrus and decreased amplitudes of bilateral N170 response to images of faces but not to images of other objects. Furthermore, there is evidence for a behavioural dissociation between schizophrenia patients with- and without delusional misidentification syndrome (DMS) in face recognition tasks. In DMS patients may mix up for example others as doppelgangers. The understanding of the pathophysiology of this condition is crucial as patients with DMS might represent a subgroup with more aggressive behaviour due to erroneous face recognition. Hence, we hypothesised reduced differences in blood oxygenation-level dependent (BOLD) response amplitudes within the FFA to images of faces and images of other objects in patients with DMS (DMS+).

Twelve schizophrenia patients according DSM-IV criteria and twelve healthy control subjects were included into the study. All groups were matches for age (mean: 27 years) and sex. Patient groups did not differ as to medication, overall psychopathology (as measured with PANSS) and duration of illness. Patients with DMS had medium up to severe degrees of illness, one patient showed a classical form of Capgras syndrome.

All participants were studied with BOLD using functional magnetic resonance imaging (fMRI) and arterial spin labelling (ASL) to measure resting perfusion. Voxel-based morphometry (VBM) analysis was used in order to compare grey-matter volume and total intracranial volume between groups. During fMRI a face-recognition task was performed in all subjects.

DMS+ patients showed less BOLD difference to images of faces and images of chairs. Only DMS+ patients showed a reduced perfusion of the right FFA at rest. We observed no differences in grey-matter volume in the right fusiform gyrus and DMS+ performed worse in the face recognition task.

We suggest that the erroneous behavioural response of patients with DMS could origin from reduced metabolism and a lack of specialisation in a region that is sensitive for the proper processing of facial information. Our data is to be discussed in context with models proposed by Ellis (2007) suggesting a dissociation of pure face features encoding and the attribution of emotional face content.

P 57 Neural correlates of catecholaminergic dysfunction as a trait abnormality in major depression

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Context: The pathophysiology of major depressive disorder (MDD) has been consistently associated with altered catecholaminergic function, especially with decreased dopamine neurotransmission, by various sources of largely indirect evidence. An instructive paradigm for more directly investigating the relationship between catecholaminergic function and depression has involved the mood response to experimental catecholamine depletion (CD).

Objective: To determine whether catecholaminergic dysfunction represents a trait abnormality in MDD and to identify brain circuitry abnormalities involved in the pathophysiology of MDD.

Design: Randomised, double-blind, placebo-controlled crossover, single-site experimental trial.

Setting: Psychiatric outpatient clinic.

Participants: Fifteen unmedicated subjects with MDD in full remission (RMDD) and 13 healthy controls.

Intervention: We induced CD by oral administration of alpha-methyl-para-tyrosine. Sham depletion used identical capsules containing hydrous lactose.

Main outcome measures: Quantitative positron emission tomography of regional cerebral glucose utilisation to study the neural effects of CD and sham depletion. Behavioural assessments included the Montgomery-Asberg Depression Rating Scale and the Snaith-Hamilton Pleasure Scale (anhedonia).

Results: Depressive and anhedonic symptoms increased during CD to a greater extent in RMDD subjects than in controls. In both groups CD increased metabolism in the anteroventral striatum and decreased metabolism in the orbital gyri. In a limbic-cortical-striatal-pallidal-thalamic network previously implicated in MDD, composed of the ventromedial frontal polar cortex, mid- and subgenual anterior cingulate cortex, temporopolar cortex, ventral striatum and thalamus, metabolism increased in RMDD subjects but decreased or remained unchanged in controls. CD-induced metabolic changes in the left ventromedial frontal polar cortex correlated positively with depressive symptoms, while changes in the anteroventral striatum were correlated with anhedonic symptoms.

Conclusions: This study provides direct evidence for catecholaminergic dysfunction as a trait abnormality in MDD. It demonstrates that depressive/anhedonic symptoms as a result of decreased catecholaminergic neurotransmission are related to elevated activity within the limbic-cortical-striatal-pallidal-thalamic circuitry.

P 58 Stress and sex hormones in alcoholics: association with treatment outcome

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Aims: Patients with alcohol dependence face a substantial risk of relapse after detoxification. Stress is a key factor for relapse, and alterations in hypothalamic-pituitary-adrenal axis and hypothalamic-gonadal axis were described. The aims of this study were to examine the course of stress and sex hormones during alcohol withdrawal and to investigate the association between these hormones and relapse in the first year after inpatient treatment.

Methods: Cerebrospinal fluid (CSF) of cortisol and testosterone, and plasma concentrations of cortisol and testosterone were investigated in 60 alcohol-dependent patients and 30 age- and sex-matched healthy controls. Blood samples for measuring plasma cortisol and testosterone were taken on the day of admission, after completion of detoxification and six weeks later. One year after discharge from inpatient treatment, outcome data on relapse were collected by face-to-face interviews.

Results: Cortisol levels-decreased and testosterone concentrations increased significantly during alcohol withdrawal. Thereafter, alcoholics showed significantly lower cortisol levels than healthy controls. There were no significant correlations between stress and sex hormones. 47% of alcohol-dependent patients relapsed in the first year after inpatient treatment. Those relapsed were characterised by higher CSF cortisol after withdrawal.

Conclusions: In alcohol-dependent patients stress and sex hormones change significantly during withdrawal. Higher CSF cortisol levels at the end of withdrawal seem to be a possible indicator for relapse during the following 12 months.

P 59 Unilateral high-frequency stimulation of the nucleus accumbens improves obsessive compulsive disorder and mood

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Background: Deep-brain stimulation (DBS) has recently been used with promising results in a small number of patients with treatment-resistant obsessive compulsive disorder

(OCD) and depression. However, little is known about prognostic factors, and the best approach for optimising stimulation parameters remains to be determined.

Method: We report a 44-year-old woman who had been operated 4 years ago for DBS of the right nucleus accumbens because of treatment-resistant OCD. Stimulation was initially judged without relevant clinical effect. Three years later, renewed systematic acute testing of stimulation allowed identification of stimulation settings that could be tolerated without side effects. Parameters leading to the best short-term improvement were first determined. Then, stimulation was re-tested under double-blind conditions to exclude a possible placebo effect: "on" stimulation, "off" stimulation and "on" stimulation at 50% reduced voltage. A neuropsychological assessment was performed in each condition using the Hamilton Depression Rating Scale (HDRS), the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the Screening List for Obsessive Compulsive Symptoms, the Questionnaire of Changes in Experiencing and Behaviour, and a VAS self- and examiner-rating of mood, motivation and interest.

Results: Mood, OCD, motivation and interest were consistently improved with stimulation, although depression and obsessive-compulsive symptoms persisted even in the best condition. The Y-BOCS rating off stimulation was 37, on stimulation 19–23, on reduced stimulation 33. The HDRS rating off stimulation was 44, on stimulation 27–35, on reduced stimulation 33. Self and examiner VAS ratings showed a marked effect of stimulation on mood, motivation and interests.

Conclusion: Unilateral high-intensity accumbens stimulation improves OCD and mood. The beneficial effect though may be only partial, and the potential additional benefit of bilateral stimulation remains to be determined.

P 60 "Football is good for your sleep." Favourable sleep-EEG patterns in young intense male football players

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Objective: Commonplace and the scientific community hold that physical activity exerts a favourable impact on sleep in adulthood. For adolescence research is scarce, although restoring sleep is crucial for psychological functioning and cognitive-emotional performance during this period of life. The aim of the present study was, therefore, to objectify by means of sleep-EEG the impact of intense football training on sleep patterns in male adolescents.

Method: Six male football players (target group) and six age- and gender-matched controls took part in the study. Mean age was 16 years, and mean intense physical activity was about 12 hours for the target group, and about 1.5 hours for the controls. Target and control groups did not differ with respect to age, school level and profiles of depressive and anxiety scores. Sleep of all 12 participants was objectively assessed with a one-electrode sleep-EEG recording. Sleep of target group was recorded during a night without exercising in the evening.

Results: Compared to controls, football players showed the following favourable sleep patterns: shortened sleep-onset time; increased sleep efficiency, less awakenings after sleep onset, and reduced stage 1. Descriptively, the target group showed shortened REM-latency, decreased light sleep and increased slow-wave sleep.

Conclusion: Results suggest that intense and regular physical activity has a favourable impact on objectively assessed sleep of male adolescents. The influence seems to be longer lasting, since sleep-EEG recording was not performed the night after intense physical activity in the evening.

P 61 Impaired glutathione synthesis in schizophrenia: convergent genetic and functional evidence

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Schizophrenia is a complex multifactorial brain disorder with a genetic component. Convergent evidence implicated oxidative stress and glutathione (GSH) deficits in schizophrenia. GSH is synthesised in two consecutive enzymatic reactions by the enzymes glutamate cysteine ligase (GCL) and the GSH synthetase (GSS). GCL consists of a catalytic (GCLC) and a modulatory subunit (GCLM). The aim of the present study was to test whether schizophrenia is associated with a deficit in GSH synthesis. As a model we selected fibroblasts that were obtained by skin biopsy. We supposed that a deficit in GSH synthesis is more pronounced under conditions of oxidative stress. We thus challenged cultured fibroblasts with tert-butylhydroquinone (t-BHQ) and we measured GSH content, GCL activity, as well as protein expression of GCLM and GCLC. Stressed cells of patients had a 26% ($P = 0.002$) decreased GCL activity as compared to controls. This reduction correlated with a 29% ($P < 0.001$) decreased protein expression of the catalytic GCL subunit (GCLC). Genetic analysis of a trinucleotide repeat (TNR) polymorphism in the GCLC gene revealed in two independent samples a significant different genotype distribution between patients and controls. The most common TNR genotype 7/7 was more frequent in controls (OR = 0.6; $P = 0.003$), while the rarest TNR genotype 8/8 was three times more frequent in patients (OR = 3.0; $P = 0.007$). Comparing functional and genetic data revealed that subjects with disease-associated genotypes had lower GCLC protein expression ($P = 0.017$), GCL activity ($P = 0.037$) and GSH contents ($P = 0.004$) than subjects with genotypes that were more frequent in controls. Taken together, the study provides genetic and functional evidence that an impaired capacity to synthesise GSH is a vulnerability factor for schizophrenia.

P 62 Age and peripheral human molecular circadian rhythms

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Suprachiasmic nucleus (SCN) cells are not the only cells that possess the oscillatory machinery of the circadian rhythm. The same molecules are also present in peripheral tissues, such as the fibroblasts, which have a cell-autonomous and self-sustained circadian rhythm. SCN tissue is difficult to obtain and manipulate, but peripheral cells such as fibroblasts have important advantages: they are easy to maintain, accessible to molecular genetic tools and can be obtained from human. Because of these advantages, fibroblasts provide an excellent alternative to the SCN in order to study the molecular and biochemical mechanisms of mammalian circadian systems in vitro. For human beings in general, circadian disturbances have been shown with age such as higher prevalence of early morning awakening and difficulties in maintaining sleep. Nevertheless, the origin of this phenomenon is unknown. In our study we addressed the question of whether fibroblasts reflect age-related differences in the circadian period length in vitro that parallel changes in subject circadian phase in vivo. For this purpose we analysed the period length of the skin fibroblasts from young and elderly subjects (young: 30 years old; elderly: 60 years old; sex-matched). In addition, we collected data about the chronotype of the subjects by analysing the Munich Chronotype Questionnaire (MCTQ). Fibroblasts were isolated from skin punch biopsies collected from the buttock of the subjects and infected with an engineered lentiviral circadian reporter (mBmal-1::luc) that permits the characterisation of circadian rhythms in vitro by bioluminescence imaging. Measurements (3 per biopsy; n = 6 total per subject) were conducted over a time period of 5 days.

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P 63 Burnout, sleep, behaviour to fall asleep and quality of life: a men's and women's domain

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Background: Commonly, burnout is studied by occupational groups and gender. However, it remains unclear to which extent burnout is predicted by gender and occupation. Moreover, the association between increased burnout and decreased sleep seems plausible, though not assessed so far with validated questionnaires.

Method: Between March 2007 and March 2008, a total of 2231 participants took part in an internet-based study. Mean age was 40.77 (SD = 10.30; 1183 females and 1048 males). They completed the Burnout Scale after Pines, Aronson and Kafry (1983), the Insomnia Severity Index (Bastien et al., 2001) and also answered to a questionnaire concerning demographics, quality of life and occupation.

Results: Applying validated questionnaires, it turned out that, irrespective of gender, burnout was highly associated with poor sleep (r = 0.64). Irrespective of gender, increased scores of burnout were correlated with dysfunctional coping styles to get asleep such as watching TV, and intake of medicaments and drugs. And again irrespective of gender, low burnout scores were reported in those participants living still at home or with a family. No association was found between burnout and occupational situation.

Conclusions: Using validated questionnaires, it turned out that burnout and poor sleep were highly correlated. Moreover, one may claim that trustful social relationships might be a protective factor against burnout. Most importantly, these patterns were completely unrelated to the occupational situation and to gender, suggesting that burnout is both a "men's and women's domain".

P 64 Do female owls have more strain than male larks? Morningness, eveningness, gender and strain among adolescents

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Background: Amongst the variety of different factors, psychological strain impairs sleep in adolescents. Moreover, there is evidence that compared to males, females report increased sleep complaints. Then, so-called chronotypes are considered genetically determined sleep/wake patterns, and three dimensions are described: morningness ("larks"), eveningness ("owls") and intermediate chronotypes. The aim of the present cross-sectional study was to describe strain in dependence of gender and chronotype.

Method: Between February and October 2007, a total of 1161 adolescents (642 females, 519 males; mean age 17.60 years ± 1.40) took part in the internet-based study. Participants completed questionnaires related to demographics, chronotypes, sleep and strain.

Results: Compared to adolescent males, females reported more to be "owls" (X2 [2] = 31.05; p <0.000). Moreover, again compared to males, females reported increased scores of strain (F [1, 1155] = 48.35, p <0.000), as well as "owls" indicated increased strain, compared to "larks" and intermediate chronotypes (F [2, 1155] = 7.31; p <0.000). Gender by chronotype interaction was not significant (F [2, 1155] = 2.52; p = 0.081), though, descriptively, "female owls" reported highest scores of strain.

Conclusion: Results suggest a complex pattern of interaction between strain, gender, and chronotype. The direction of influence remains unclear: Does a genetically determined tendency to sleep delay and morning sleep ("owls") lead to conflicts with socially determined sleep/wake schedules, and therefore to decreased daily performance and increased strain? Or does "only" sleep loss lead to decreased daily performance and to heightened strain? And why should female adolescents be particularly susceptible to eveningness and to strain?

P 65 Does daily physical activity have a beneficial effect on psychological functioning in children and adolescents with cleft lip and palate (CLP) compared to healthy controls?

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Objective: A wealth of research shows that physical activity exerts a favourable impact on psychological functioning. However, for childhood and adolescence research is mixed, and with respect to children and adolescents after cleft repair, findings are completely missing. The aim of the present study was therefore to investigate the impact of daily physical activity on psychological functioning in children and adolescents after cleft repair, and to compare these data with those of healthy controls.

Methods: Thirty-two children and adolescents with CLP, and 34 controls were recruited. Ages ranged from six to 16 years. For psychosocial assessment the Strength and Difficulties Questionnaire (SDQ) was completed. Moreover, participants indicated the amount and the intensity of daily physical activity during seven consecutive days.

Results: Daily physical activity was positively associated with favourable psychological functioning. This pattern did not differ between participants with and without CLP. Moreover, this pattern was not age and gender related, that is to say: daily physical activity had the same favourable impact on children and adolescents, irrespective of gender.

Conclusions: Findings are in line with the host of studies, which underlines the favourable impact of regular physical activity on psychological functioning. Importantly, daily physical activity had beneficial effects on participants both with and without CLP repair, irrespective of age and gender.

P 66 Hypericum perforatum for depressive and somatoform symptoms – a field report for the efficacy and tolerability of a standardised extract of Hypericum perforatum

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Background: Beneficial effects of Hypericum perforatum on depressive and somatoform disorders have been demonstrated repeatedly.

Questions: The field report aimed at highlighting the beneficial effects on both depressive and somatoform symptoms for different ages of patients, and the importance of concomitant medication.

Methods: A total of 725 patients were interviewed by questionnaires at the beginning and at the end of treatment with hypericum. Treatment lasted from four to six weeks.

Results: Beneficial effects of hypericum on both depressive and somatoform symptoms were observed independently of age and gender. Patients with highly increased depressive and somatoform scores needed concomitant medication. Satisfaction with efficacy reached 88%, and satisfaction with tolerability reached 98%.

Conclusions: Independently of age and gender, hypericum is very well tolerated and regarded highly effective for both mild to moderate depressive and somatoform symptoms. Patients suffering from more severe symptoms seem to need concomitant medication or a switch to synthetic antidepressive medication.

P 67 Increased cortisol secretion in Swiss Army recruits suffering from anxiety to wear the protective mask compared to controls

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Background: Difficulties to wear protective gears and protective clothing are common

among military personnel, fire fighters or disaster relief workers. However, quickly and correctly wearing the protective mask dramatically increases survival. Difficulties to breathe, sweating, extreme sensation of tightness and panic attacks are reported as an anxiety to and the reaction of wearing the protective gear. Reactions may meet the criteria of a specific phobia. We investigated the cortisol secretion before and after cognitive-behavioural treatment of this specific phobia in Swiss Army recruits and compared these data with those of healthy controls.

Method: A total of 35 Swiss Army recruits suffering from specific phobia to wear the protective mask took part in the study (target group). Salivary cortisol was assessed under exposure conditions before and after cognitive-behavioural treatment (CBT). CBT lasted 12 hours. Moreover, morning salivary cortisol was analysed. Data were compared with those from healthy controls, that is to say, from 28 Swiss Army recruits of a disaster relief squad.

Results: Compared to controls, the target group showed an increased cortisol secretion before and after CBT. Morning cortisol was also increased. Within the target group, cortisol secretion under exposure conditions decreased after CBT.

Conclusions: The anxiety to wear a protective mask meets the DSM-IV criteria of specific phobia and is mirrored by increased HPA-axis activity, that is to say, with increased cortisol secretion. Within 12 hours CBT reduces cortisol secretion.

P 68 Is the increase of hypomanic stages during adolescence gender and developmental task related?

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Objectives: Hypomanic states are observable among patients suffering from bipolar II and minor bipolar disorders, and in nonclinical samples. Furthermore, there is evidence that females may be at risk for developing affective disorders. We studied hypomanic stages in adolescents, focusing on active/elated and risk-taking/irritable hypomania scores and on gender.

Methods: Of 107 adolescents (mean age: 17.98, SD = 1.33) sampled, 60 indicated they experienced intense romantic love, while 47 had a longer-lasting relationship or were singles. Following a screening interview for psychiatric disorders, participants completed the Hypomania Check List (HCL-32; Angst et al., 2005). Their data were compared with those of adult patients suffering from bipolar II disorders.

Results: Scores of adolescents in intense romantic love did differ from those of controls, but not from those of patients suffering from bipolar II disorders. Comparisons of factor analytic scores revealed that both groups of adolescents displayed higher overall scores for the factor irritable/risk-taking hypomania. Furthermore, a gender-related pattern was found, with greatly increased scores for female adolescents.

Conclusions: In professional contexts adolescents' developmental tasks surrounding experiences in social, psychosexual and substance use-related engagement will be encountered. These experiences may lead to temporarily and gender-dependent hypomanic-like stages.

P 69 Neuere therapeutische Ansätze in der Behandlung des Alkoholmissbrauchs

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Das zunehmende Wissen über die Neurobiologie süchtigen Verhaltens hat zur Entwicklung neuer Pharmakotherapien des Alkoholismus geführt. Evidenzbasierte Aussagen sind möglich: zur Rückfallvermeidung (d.h. Abstinenzerhaltung nach vorangegangenem Entzug), zur Minderung der Rückfallschwere sowie zum Verbleib von Alkoholabhängigen im Behandlungsprogramm (Compliance). Die meisten Medikamente, die für die Indikation Alkoholabhängigkeit getestet worden sind, verfehlten den Wirksamkeitsnachweis. Ausnahmen sind Acamprosat und Naltrexon. Beide werden zur adjuvanten Pharmakotherapie eingesetzt. Beide sollten über 12 Monate eingenommen und bei einem Rückfall nicht abgesetzt werden. Nach Entgiftung erhöht Acamprosat signifikant die Abstinenzwahrscheinlichkeit. Ausserdem konnte gezeigt werden, dass Acamprosat einen positiven Effekt auf das Verbleiben von Alkoholabhängigen in der Therapie hat. Bezogen auf die Behandlungsziele der Rückfallvermeidung, der Rückfallverkürzung und des Verbleibs in ambulanter Therapie, bestehen für Acamprosat moderate, aber statistisch signifikante Wirksamkeiten, die zwischen 7 und 13% über dem Plazebo-Effekt lagen. Naltrexon ist für die Indikation Rückfallprophylaxe bei Alkoholabhängigkeit nicht zugelassen. Es kann deshalb nur nach den Bedingungen eines «off-label use» verordnet werden. Es besteht ein gesicherter Effekt bei der Rückfallverkürzung. Darüber verringert Naltrexon statistisch signifikant das Risiko, dass sich erneutes Trinken zu einem schweren Rückfall ausweitet. Ein Effekt auf den Verbleib von Alkoholabhängigen in ambulanter Behandlung konnte nicht nachgewiesen werden. Naltrexon hat auch eine signifikante Wirkung auf den Abstinenzerhalt. Die ehemals grosse Popularität des Vergällungsmittels Disulfiram konnte bis heute durch Studienergebnisse nicht gerechtfertigt werden.

P 70 Neuroleptic medication in schizophrenic patients increases intracerebral EEG connectivity (sLORETA-based lagged coherence)

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The disconnection syndrome of schizophrenia in medication-naive, acute patients exhibits the EEG characteristics of decreased functional connectivity (coherence) between brain regions, increased 'chaotic' dimensionality (correlation dimension) and shortened microstate durations. Accordingly, medication is hypothesised to reverse the aberrations. We tested this hypothesis examining coherence, one of the three parameters, separately for each of the 8 EEG frequency bands. Since conventional coherence ('total coherence') is uncontrollably enhanced by volume conduction, we used 'lagged coherence' that omits zero phase lag, thus only measuring connections with time delay between regions (which can be interpreted as true functional connectivity). Also, since raw scalp EEG data cannot directly be read as localisation, we used sLORETA-computed intracerebral waveshapes for analysis. Artifact-free EEG (mean 182 ± 89 seconds/patient) from 37 schizophrenics under neuroleptic medication was available (age 37.7 ± 9.2 years, 19 men). Medication dosage during 10 days before the EEG recording was assessed in chlorpromazine equivalents CPZE (mean 311 ± 308 CPZE/day/patient). Current density at the 6239 sLORETA voxels/time frame was used to compute time series of 19 intracerebral regions (ROIs) corresponding to the cortex underlying the 10/20 scalp electrode schematic. Lagged coherences were computed between all regions for each of the 8 EEG frequency bands and were correlated with CPZE across patients. For the 8 bands 60 lagged coherences correlated at $p < 0.05$; 98% (59) of these increased (53 in theta) with increasing dosage, while only 2% decreased. Conventional coherence on the scalp yielded completely different results: 158 correlated at $p < 0.05$; 37% (59) increased with increasing dosage (16 in beta1), but 63% (99) decreased (45 in alpha2); conventional coherence ('total coherence') between the intracerebral ROIs showed comparable results (19% increased, 81% decreased).

In sum: As hypothesised, increasing dosage of neuroleptic medication produced a dose-dependent increase of interregional brain functional connectivity in the cortex of schizophrenic patients (mostly in the EEG theta frequency band), when distorting effects of volume conduction were excluded by computing lagged coherence.

P 71 Perceived parenting styles, personality traits and sleep patterns in adolescents

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Background: Amongst the variety of different factors, psychological strain impairs sleep in adolescents. Moreover, adolescents get increasingly independent from their parents. However, the impact of parent's behaviour on adolescents' psychological functioning and sleep has remained unclear. Therefore, the present study examined the role of parenting styles with respect to adolescents' sleep patterns and symptoms of depression and anxiety.

Method: A total of 246 adolescents (age: 17.58 ± 1.62) took part in the study. They completed several questionnaires with regard to parenting styles and to symptoms of anxiety and depression; additionally, they filled in a questionnaire assessing sleep-related personality traits and completed a sleep log for seven consecutive days.

Results: Findings showed a high overlap between parenting styles of both parents, though with a different impact on adolescents' sleep. Adverse parenting styles were highly correlated with low sleep quality, negative mood, increased daytime sleepiness and with increased symptoms of anxiety and depression. Adolescents with low positive and high negative parenting styles displayed the most unfavourable sleep-related personality traits.

Conclusions: Results suggest that parenting styles may have an impact on young people's sleep pattern even at the beginning of late adolescence. Moreover, adolescents seem far from getting emotionally independent from their parents.

P 72 Polysomnographic profiles of patients suffering from restless legs syndrome, depressive symptoms and major depression are not gender related

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Objectives: Amongst the variety of disorders affecting sleep, depressive disorders and restless legs syndrome (RLS) demand particular attention. Sleepiness, daytime fatigue, cognitive deficits and loss of interest are symptoms attributable to both depressive disorder and RLS. Moreover, beside the overlap of symptoms, a high co-morbidity rate is observed. However, onset of RLS seems to precede onset of depressive symptoms. Surprisingly, no study so far has addressed this issue using sleep EEG. Moreover, there is evidence that females are at increased risk for developing sleep disorders in general, and RLS in particular.

Methods: We retrospectively compared polysomnographic recordings of outpatients with RLS (n = 25; age 53.32 ± 16.23), RLS and depressive symptoms (n = 38; age 50.20 ± 14.42), and inpatients suffering from major depressive disorders (n = 15; age 51.47 ± 8.04).

Results: Results showed that both groups with RSL had lower sleep efficiency, compared to the group with major depressive disorder. Most disturbed sleep continuity was observed in the group with RLS and depressive symptoms as a possible additive effect. Furthermore, RLS not only seems to precede onset of depressive symptoms, but because of overlap of symptoms, RLS also may lead to unfavourable overmedication: outpatients with RLS and depressive symptoms were twenty times more likely to be pre-treated with antidepressants, before being diagnosed as RLS. No gender-related sleep patterns could be observed.

Conclusions: Overall, the impact of RLS seems to be underestimated in community health care, and primary-care physicians should be instructed to explore RLS. Moreover, applying objective sleep-EEG measurements, no gender-related gap could be observed.

P 73 Psychosocial functioning and sleep patterns in children and adolescents with cleft lip and palate (CLP) compared to healthy controls

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Objective: The aim of this study was twofold: to assess psychological functioning, interactional competencies and sleep patterns in children and adolescents with cleft lip and palate (CLP); to compare these results with those from age- and gender-matched controls. It was hypothesised that participants with CLP would show increased difficulties in psychological functioning, more interactional difficulties and poorer sleep patterns.

Methods: Thirty-two children and adolescents with CLP, and 34 controls were recruited. Ages ranged from six to 16 years. For psychosocial assessment the Strength and Difficulties Questionnaire (SDQ) and a questionnaire on interactional competencies (PIELCQ) were completed; for sleep assessment a sleep log was completed for seven consecutive nights.

Results: Participants with and without CLP did not differ with respect to emotional problems, conduct problems or hyperactivity. With respect to interactional competencies, participants with CLP were six times more likely to report difficulties. Unfavourable sleep patterns were associated with psychosocial strain, but not with the presence of CLP.

Conclusions: Results indicate that children and adolescents with CLP may complain about sleep irregularities as much as people without CLP. In adolescence, the presence of CLP may cause increased difficulties. Consequently, skill training to improve context-related social competencies may be appropriate.

P 74 Resting EEG-based intracortical functional connectivity in Alzheimer's disease and frontotemporal degeneration

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Identifying the specific cause of dementia is increasingly important as disease-specific medications have become available. The electroencephalogram (EEG) is a suitable tool that could help clinicians to differentiate frontotemporal dementia (FTD) from Alzheimer's disease (AD). AD patients show a decreased functional connectivity compared to healthy controls (e.g., Jelles et al., Clin Neurophysiol, 2008) as well as compared to patients with FTD (Pijnenburg et al., Clin Neurophysiol, 2008). All previous connectivity studies focused on scalp EEG data and have the limitation that they cannot account for localisation. The only way to obtain functionally interpretable information on connectivity of EEG signals between brain regions is to model the scalp-recorded data by intracerebral generator sources and to compute connectivity between the time series of source strengths of these model sources (Lehmann et al., J Physiol Paris, 2006). Here we recorded resting-state EEG (19 channels) from two groups of mild to moderate AD (n = 21) and FTD (n = 16) patients and a group of age-matched healthy controls (n = 17). sLORETA (Pascual-Marqui et al., Methods Find Exp Clin Pharmacol, 2002) was applied to calculate the source strengths of the intracortical generators in nine regions of interest (ROI, frontal left/right, temporal left/right, central, parietal left/right, occipital left/right) and in the seven classical frequency bands. A 3-way ANOVA with group as between-subject factor and ROI and frequency bands as within-subject factors revealed a significant interaction between group × frequency bands × ROI ($F = 1.7$; $p < 0.0001$). Post-hoc analyses (t-statistics) confirmed a significantly decreased connectivity in AD relative to healthy controls in the alpha1 band (8.5–10 Hz). Also, AD showed a significantly de-

creased connectivity compared to FTD in the alpha1 and in the theta (6.5–8 Hz) frequency bands. The decreased connectivity in AD relative to the two groups concerned the whole brain, suggesting a generalised loss of functional interactions between the different brain regions in AD. In line with previous reports (e.g., Pijnenburg et al., Clin Neurophysiol, 2008) which found no detectable deviations of EEG parameters in FTD in spite of widespread neuronal degeneration, our study's EEG intracerebral connectivity remained in the normal range during mild-to-moderate stages of the disease. The present results demonstrate that EEG adds important information that increases diagnostic confidence.

P 75 Scalp EEG connectivity and intracerebral electrical connectivity (sLORETA-lagged coherence) during resting and meditation

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In meditators of four traditions (13 Tibetan Buddhists TB, 15 QiGong QG, 14 Sahaja Yoga SY, 14 Ananda Marga Yoga AY) we studied brain electric functional connectivity during wakeful resting before (rest1) and after (rest2) tradition-specific meditation (self-dissolution, QiGong, Samadhi). 19-electrode EEG was recomputed via sLORETA current density (6239 voxels) into intracerebral waveshapes of 19 intracerebral regions (ROIs) corresponding to the cortex underlying the 10/20 electrode schematic. Functional connectivity was computed as conventional coherence ('total coherence') from the scalp-recorded data and as 'lagged coherence' from the sLORETA-based waveshapes (lagged coherence omits zero phase lag, thus only measuring connections with time delay; these are interpretable as true functional connectivity). For each meditator group t tests identified significant coherence differences between rest1 and rest2 versus meditation in each of 8 EEG frequency bands (delta to gamma). Between 19 electrodes (or ROIs) there are 171 connections; in each subject and frequency band all connections were counted that reached significant different coherence between rest1 and rest2 versus meditation. Summing significant cases in TB, QG, SY and AY across all 8 bands, using scalp coherences, in the four traditions between 0 and 3% of the connections were significantly higher in meditation than rest, between 6 and 16% lower; using intracerebral lagged coherence, 0% were higher, but between 26 and 61% were lower. On average across the four traditions, scalp coherence decreased most strongly in alpha1 and 2 and beta1 and 2, while intracerebral-lagged coherence decreased most strongly in delta, theta and beta1 and 2. For the gamma frequency band alone scalp coherences were higher between 1 and 13%, lower between 1 and 6%; intracerebral-lagged coherences were higher in 0%, lower between 2 and 75% of cases. – Thus, all four traditions clearly showed more significant decreases than increases in scalp coherence, and only significant decreases, no increases in intracerebral-lagged coherence that avoids distorting volume conduction. Contrary to reports of strongly increased gamma coherence in meditation, averaged across our four traditions, in scalp coherence only 5% of the gamma band coherences significantly increased, 4% decreased, while in intracerebral-lagged coherence none increased but 38% decreased.

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P 76 Sleep-spindle activity in depressed patients: association with cognitive performance and REM-density

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Objective: There is increasing evidence that sleep spindles are linked to memory-encoding processes and seem to reflect important aspects of efficient cortical-subcortical connectivity. This study investigated if levels of sleep-spindle activity are associated with cognitive impairment during depression.

Method: 10 patients (mean age 50.5 ± 8.8 years) with a major depressive episode were treated with trimipramine 200 mg/d over six weeks. Polysomnography was performed after one week of treatment. Visually scored sleep spindles were correlated with depression severity (HDRS) and cognitive-psychomotor performance, as assessed with a comprehensive test battery, after one, two and six weeks of treatment and at follow-up 4.0 ± 2.75 years later.

Results: Higher levels of sleep-spindle activity were significantly correlated with better psychomotor-cognitive performance on all test sessions. Lower levels of sleep-spindle activity were associated with increased REM density. Both spindle activity and cognitive performance were not correlated with depression severity.

Conclusions: Our data suggest that lower sleep-spindle activity is associated with impairment of attention, complex information processing and psychomotor coordination in depressed patients. The association between reduced spindle activity and elevated REM-density in depression points to putative common pathophysiological pathway, e.g. enhanced cholinergic activity in pontine nuclei. If the level of sleep-spindle activity during depression may serve as a predictive marker for antidepressive treatment response has to be investigated in a larger sample and follow-up studies.

P 77 Sleep spindles in kindergarten children: relation to sleep macrostructure and hypothalamic-pituitary-adrenocortical (HPA) activity

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Introduction: Sleep regulation and HPA activity are closely associated to each other and are essential to psychiatric disorders like depression. However, there is little knowledge about the association of sleep microstructure, e.g. sleep spindles, to sleep macrostructure and to stress regulation. Especially sleep spindles have been linked to efficient cortical-subcortical connectivity and cognitive abilities during neurodevelopment.

Aim: In order to investigate in these relationships in the stage of early development, HPA activity and sleep regulation were analysed in kindergarten children. The results were put in relation to sleep microstructure.

Patients and methods: Forty-one five-year-old kindergarten children were enrolled in a cross-sectional examination of HPA-system activity assessed by saliva-cortisol measurements (morning cortisol after awakening) and sleep regulation investigated by sleep EEG-monitoring. Sleep EEG spindles were visually scored and put into relation to macrostructural sleep and HPA-activity parameters.

Results: Sleep spindles were correlated to morning-cortisol secretion (AUC total; curvilinear $r = 0.56$; $p < 0.01$). Besides, a negative correlation was found between sleep spindles and REM-sleep time (curvilinear $r = -0.46$; $p < 0.05$) and REM density ($r = -0.45$; $p < 0.05$) respectively. There was a significant negative correlation between awakening cortisol (AUC total) and REM-sleep time.

Conclusion: Not only macrostructure but also microstructure of sleep is associated to HPA-axis regulation. Whether these parameters are correlated to psychological and cognitive variables is now subject of a further follow-up study.

P 78 The impact of mothers' behaviour on infants' sleep before and after surgical intervention for cleft-lip-palate (CLP) repair

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Objectives: Next to cardiovascular and genitourinary malformations, CLP is the most common congenital defect demanding sur-

gical repair. In Europe about one in 700 births is affected by a CLP malformation. The commonplace view is that any surgical intervention in young infants leads to heightened psychological and physiological stress – in both infants and parents. However, reliable data are missing. Furthermore, if the surgical intervention was a stressful event, this should be mirrored in changes to the child's sleep continuity. The aim of the study was therefore to assess sleep of infants with CLP before and after CLP repair, and to compare these sleep patterns descriptively with the mothers' sleep pattern.

Methods: The sleep of seven infants with CLP was assessed by means of actigraphy four days before and four days after surgical intervention for CLP repair. Additionally, mothers completed a sleep log for the same period of time.

Results: No statistically significant differences between infants' sleep before and after surgical intervention were observed. Infants' sleep duration decreased markedly the night before the surgical intervention. Mothers' sleep quality decreased preceding the day of the CLP repair, and sleep-onset latency almost doubled.

Conclusions: CLP repair is not as traumatic as the commonplace view holds, because otherwise infants' sleep patterns would have been much more altered. However, comparing the patterns of mothers' and infants' sleep suggests that infants are sensitive to their mother's psychological tension and behaviour. As a result, infants may become concerned, and this tension is reflected in reduced sleep.

P 79 The myth of the beauty sleep – revisited

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Background: There is a wealth of myths and legends concerning sleep. Among those commonplace holds that sufficient and restoring sleep has a beneficial effect on beauty – the beauty sleep. However, no reliable data are available, and one might claim that this myth is a "women's domain". A second myth regards the claim that daytime performance is closely associated with restoring sleep. The aim of the present study was therefore to explore to which extent beauty and daily performance are thought to be connected to sleep in dependence of gender and chronotypes.

Method: Between February and October 2007, a total of 957 adolescents (532 females, 425 males; mean age 17.60 years ± 1.40) took part in the internet-based study. Participants completed questionnaires related to sleep.

Results: Compared to adolescent males, females were more convinced that restoring sleep has a beneficial effect on beauty ($F[1,955] = 32.47, p < 0.000$). Moreover, evening-ness chronotypes were convinced that restoring sleep has a beneficial effect on beauty ($F[1,955] = 6.59, p < 0.001$). However, gender by chronotype interaction showed that female morningness chronotypes were most convinced that beauty depends on restoring sleep. With regard to daily performance, the factors gender or chronotypes were not significant ($F < 1.5$). However, female morningness chronotypes were significantly more convinced that restoring sleep improves daily performance.

Conclusion: The myth of the beauty sleep seems to currently persist in female adolescents, and above all in those female adolescents who go to sleep early and stand up early in the morning. Importantly, these female adolescents were also most convinced that restoring sleep improves daily performance. Data suggest that female adolescents might be particularly sensitive to sleep.

P 80 Transgenic mouse models of Alzheimer's disease: from proteomics to functional assays of mitochondria

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Background: Alzheimer's disease (AD) is the most frequent form of dementia among the elderly and is characterised by neuropathological hallmarks of extracellular amyloid plaques and intracellular neurofibrillary tangles in the brain of AD patients. Amyloid plaques are composed of the amyloid-beta (Aβ) protein, derived from its precursor protein APP. Neurofibrillary lesions are formed from paired helical filaments composed of hyperphosphorylated tau protein, a microtubule-associated protein. Importantly, current data indicate a complex relation between the amyloid pathology and pathology involving microtubule-associated protein tau during disease. Based on our previous findings, we hypothesise a direct impact of abnormally phosphorylated tau and Aβ on proteins/enzymes involved in energy metabolism and mitochondrial respiratory chain.

Methods: For this approach we are currently investigating the brains of double (APP [KM670/671NL] / PS2 [N141I]), triple (APP [KM670/671NL] / PS2 [N141I] / Tau [P301L]) and single Tau (P301L) transgenic mice at the age of 2, 4, 7–8, 12 and 16 months. Proteomics studies are combined with functional analysis of mitochondria. Mitochondrial respiration is studied with a high-resolution respirometry system (Oxygraph-2k). In addition, enzyme activities of complexes I and IV will be determined with spectrophotometric and colorimetric assays. ROS levels, mitochondria-membrane potential and ATP levels are determined in cortical brain cells from the mice using fluorescence and bioluminescence assays.

Results: We have first ex-vivo evidence of relationship between Aβ and/or tau pathologies and alterations of mitochondrial function. Indeed, in triple transgenic mice mitochondrial function is reduced compared to double transgenic mice and to single transgenic tau mice. In fact, activities of mitochondrial complexes I and IV were decreased as well as membrane potential and ATP levels. On the contrary, ROS production increased. These effects seem to be age dependent and correlate with the corresponding Aβ and tau histopathologies.

Conclusions: Based on these findings, we conclude that tau pathology involves a mitochondrial and oxidative stress disorder distinct from that caused by Aβ. Moreover, we hypothesise that both Alzheimer's proteins, tau and Aβ, seem to act in a synergistic or additive way on proteins/enzymes involved in energy metabolism and on mitochondrial respiration chain function leading to/accelerating neurons demise.

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P 81 "Fit for high performance and fit for sleep!" Adolescent competitive athletes show favourable sleep-related personality traits and low intake of psychoactive drugs compared to controls

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Background: Chronic sleep disturbances appear already during adolescence. Often, intake of substances such as alcohol, cannabis or medicaments is aimed at reducing difficulties to fall asleep or at maintaining sleep; consumption of coffee or nicotine is aimed at decreasing daily sleepiness. In comparison, daily physical activity is considered an easy, and time- and costs-saving method to prevent or treat sleep disturbances. Scientific data, however, are scarce. Therefore, we tested the hypothesis that adolescent competitive athletes show reduced intake of substances and show favourable personality traits, if compared to controls.

Methods: A total of 258 adolescent competitive athletes (139 females, 119 males; mean intense physical activity/week: 14 hours) and 176 controls (139 females, 37 males; mean physical activity/week: six hours) took part in the study. Mean age was 17 years. Participants completed a series of questionnaires with regard to the consumption of psychoactive substances and sleep.

Results: Compared to controls, competitive athletes had significantly lower intake of

nicotine, alcohol and cannabis. Cannabis and medicaments were significantly less used to induce sleep. Moreover, competitive athletes showed increased scores of self-worth and lower scores of rumination. Additionally, they reported increased sleep quality.

Conclusions: Findings suggest that compared to controls, intense regular physical activity leads to favourable sleep and sleep-related personality traits, and decreases intake of psychoactive substances.

P 82 "Football is good for your sleep." Evidence of positive associations between regular sports and sleep in male adolescent football players

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Objective: Commonplace and the scientific community hold that physical activity exerts a favourable impact on sleep in adulthood. For adolescence research is scarce although restoring sleep is crucial for psychological functioning and cognitive-emotional performance during this period of life. The aim of the present study was, therefore, to investigate the impact of regular football training on sleep patterns in adolescents.

Method: A total of 36 male regular football players and 34 controls (mean age: 16 years; average time spent for physical exercise per week was 12 hours for the regular football players and 1.5 hours for the controls). Exercising consisted of four training sessions and an official game on a weekend day. Participants were controlled for educational level, and for depression and anxiety scores. They completed a sleep log for seven consecutive days.

Results: Compared to controls, regular football players reported significantly shorter sleep-onset latency (SOL), less awakenings after SOL and higher scores of sleep quality and mood. They referred higher scores of concentration and lower scores of tiredness during the day. The variability of sleep duration and bedtime from weekday to weekend was significantly smaller among regular football players when compared to the control group.

Conclusions: The study's findings suggest that for male adolescents regular sport is positively associated both with quantitative and qualitative dimensions of sleep. Moreover, regular physical activity on weekends such as playing football games seems to reduce unfavourable variations of sleep duration and bedtime on weekends.

P 83 "Oh, Baby, please don't cry!" Osteopathic treatment reduces crying intensity and duration in infants with colic, compared to treatment as usual

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Background: Infantile colic affects 8–40% of infants and causes distress both to the child and the parents. Generally, infantile colic is defined following Wessel's "Rule of Threes", that is to say: crying at least or more than 3 hours per day, on more than 3 days per week, for more than 3 weeks. In general, a lack of aetiology and consensus of treatment is observed. Treatment as usual (TAU) consists of thorough medical check to exclude possible concomitant illness and of behavioural advice such as rocking, walking or frequent feeding. Osteopathic treatment (OT) is a complementary therapy. In short, osteopathic treatment consists of the diagnosis of the musculo-skeletal strain patterns in the body, followed by techniques to release these strains. The aim of the study was to compare TAU and OT with regard to infantile colic (IC).

Method: A total of 16 infants (mean age: 8 weeks; range: 2–12 weeks) were prospectively enrolled in the study. First, all infants underwent thorough medical check and IC was diagnosed. Afterwards, they were randomly assigned either to TAU or OT. Ten infants entered the OT branch; six were assigned to the TAU branch. OT consisted of four sessions within four weeks; infants in the TAU branch received no further treatments. After four weeks, all infants were thoroughly examined and assessed again. Parents completed several questionnaires with regard to family strain, crying intensity and duration, and sleep, before and after OT or TAU.

Results: Baseline: Infants of the two groups did not differ with respect to gender, age or birth weight. Likewise, mothers did not differ with respect to age, vocational career, education, quality of pregnancy or any further perinatal conditions. Pre-post-comparison: Compared to infants of the TAU group, crying intensity ($F [1, 14] = 4.58$; $p < 0.05$) and duration ($F [1, 14] = 4.78$; $p < 0.05$) decreased significantly in infants of the OT group. Overall family strain decreased for all families irrespective of group ($F [1, 14] = 4.40$; $p < 0.05$), though with significant strain reduction for families with infants of OT ($F [1, 14] = 4.96$; $p < 0.05$). No significant results were observed with respect to sleep.

Conclusions: Infantile colic causes both the infant and the family system distress. Osteopathic treatment successfully reduced crying intensity and duration in the infant and significantly relieved family strain.

P 84 Insomnia in the Swiss population – causes and treatments

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Introduction: We have previously reported the results of a sleep survey study in Switzerland showing that 31% of interviewed sample (N = 1002; age 18–75) suffer from insomnia (DSM-IV criteria) of various severity (Delini-Stula et al., 2007). We here report the results of the analysis of the causes and of the treatment attitude of the interviewed sample.

Methods: The details of the method have previously been described (Delini-Stula et al., 2007). Briefly, a specifically constructed questionnaire (80 items) was addressed (telephone interview, computerised CATI system) to a random sample of subjects of both sexes. The recorded responses were systematised (using DSM-IV definitions of insomnia) and transformed into numerical and categorical values if appropriate, or expressed in percentages of observations. The results were descriptively analysed. Chi-square and other non-parametric statistical tests were applied if appropriate.

Results: Six main causes of insomnia (median n of symptoms ≥ 3) were identified in the analysed sample (N = 1002; both sexes; age 39.5 ± 15.18): personal and professional problems, diseases (psychic, somatic), life style (alcoholism), environmental factors and financial problems. Whereas personal/professional problems were the most frequent cause of less severe sleep disturbances, psychic and somatic problems were dominant factors in severe insomnia. More than 80% of insomnia subjects reported never to use any treatment. Only about 40% of severe insomniacs used prescribed drugs. Also, of the whole population only 44% believed in the efficacy of the hypnotics, but 56% thought that herbal products are an effective treatment.

P 85 Redox dysregulation and increased oxidative stress during early brain development in mice: an animal model of schizophrenia

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Glutathione (GSH) deficit combined with elevated dopamine (DA) during development leads to reduced parvalbumin (PV) expression in a subclass of GABA interneurons and abnormal dendritic spine morphology in rat anterior cingulate cortex (ACC). Similar changes are found in post-mortem brain tissue of schizophrenic patients. GSH is a

major redox regulator that is decreased in patients' cerebrospinal fluid and prefrontal cortex. Additionally, the gene of the key GSH-synthesising enzyme, glutamate-cysteine ligase modifier (GCLM) subunit, is associated with schizophrenia. We hypothesise that GSH dysregulation, by increasing vulnerability to oxidative stress, could be involved in the manifestation of morphological anomalies in the schizophrenic brain. In the present study we use a GCLM knock-out (KO) mouse model that presents with ~50% decreased brain GSH levels. During development a subgroup of animals is exposed to elevated oxidative stress induced by treatment with the DA reuptake inhibitor GBR12909. Results reveal a genotype-specific delay in cortical PV expression at postnatal day (P)10 in GCLM-KO mice as compared to wild-type. At P16, PV expression remains reduced in GCLM-KO ACC; this effect is stronger in animals that are treated with GBR from P5 to P10. GBR12909 treatment during a later developmental stage (P10–20) results in a less pronounced PV expression deficit at P20. Our results suggest that the expression of PV-positive GABA interneurons is particularly vulnerable to increased oxidative stress during a distinct developmental period (P5–10). These preliminary results add experimental evidence for the crucial role of intact redox regulation during cortical development.

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