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Abstracts
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Freie Mitteilungen

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FM 1 Motor imagery in older adults, a new way to assess higher-level gait and balance disorders

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Objectives: To measure and compare the time needed to complete the Timed Up & Go test (TUG), the time needed to imagine performing the same test (iTUG) in a sample of young and older adults, and to examine whether there was an association between the Timed Up & Go test results (TUG and iTUG), age and cognitive decline.

Methods: This study included 162 subjects (38 healthy young adults, mean age 25.7 ± 2.3 years, 73.7% women and 124 older inpatients, mean age 85.3 ± 6.5 years, 76.6% women). The mean ± SD of TUG and iTUG, age and the Mini Mental State Examination (MMSE) score were used as outcomes. The height, the number of drugs taken per day, the use of psychoactive drugs, the use of a walking aid and a history of falls in the previous year were used as covariables.

Results: Older adults performed the TUG slower than young adults ($P < 0.001$), as the imagined TUG ($P < 0.001$). Multivariate linear regressions showed that age was associated with an increase in time of TUG ($P < 0.001$) and with a decrease in time of iTUG ($P < 0.001$). There was an increase in time of TUG ($P < 0.001$) for subjects who used a walking aid and who fell in the previous year.

Conclusion: These results provide the first evidence that iTUG is clinically feasible among frail older adults and may quickly contribute to assess higher-level changes in control of gait and balance in older adults.

FM 2 Multicentric tumor manifestations of high grade gliomas: independent proliferation or hallmark of extensive disease?

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Objective: Improvements in microneurosurgical techniques, radiotherapy and chemotherapy for high grade gliomas result in better local tumor control and longer progression free survival. Multicentric (MC) lesions located distant from the initial resection area, contribute to treatment failure in a growing number of patients. These MC lesions may develop within the course of the disease (metachronous) or may already be present at the time of first tumor manifestation (synchronous). To look for mechanisms and regular patterns behind MC glioma manifestations and to investigate whether they are "a second primary tumor" or the result of continuous diffuse glioblastoma cell invasion, we retrospectively analyzed the initial and all follow up MR studies of our high grade glioma (HGG) patients.

Patients and methods: MR studies of 247 consecutive patients treated for HGG at a single institution were analysed. MC tumor manifestation was defined as more than one gadolinium enhancing lesion within the brain on MRI without a connecting signal alteration in T2 sequences and/or without a connecting hypointense mass in T1 sequences. The minimal distance to define two solitary lesions was set at >10 mm. The MR studies were retrospectively analyzed for patterns in MC tumor manifestation and progression. Topographical specifications and delay in manifestation were used to explain possible pathways of development. Kaplan Meyer survival graphs for metachronous and synchronous MC disease were calculated.

Results: According to specifications 40 patients showed MC tumor manifestations in their MR studies on admission or during treatment of their disease. 24 patients showed MC tumor manifestation at the time of admission. 16 of the cases developed MC manifestation within a follow up period of 3 to 57 months. The location of all lesions could be categorized into three distinct patterns (white matter, subependymal, intraventricular). The patterns showed individual and location specific time gaps to metachronous manifestation.

Calculated from the time of first tumor diagnosis, the median survival was longer for patients with metachronous MC lesions (353 days, $p < 0.05$) compared to patients with synchronous MC lesions (110 days) or patients without multicentricity (234 days). Patients with metachronous lesions showed similar survival (72 days) as patients with synchronous MC lesions (110 days) once they developed MC disease.

Conclusion: The topographical patterns and temporal characteristics of MC disease suggest that all manifestations share common mechanisms such as an active migratory process. Our data therefore do not support the concept of an independent MC development of multiple gliomas.

FM 3 Stress hormones to predict cerebrovascular Re-events in TIA patients

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Background: Transient-ischemic-attack (TIA) is a strong predictor of subsequent stroke. It has been shown that copeptin, a hypothalamic-stress-hormone, is an accurate prognostic marker in acute stroke. This study assessed prognostic reliability of two distinct stress hormones, copeptin and cortisol, for the risk-stratification of re-events in TIA-patients.

Methods: We conducted a prospective study in patients admitted to the emergency department with acute TIA. Clinical risk scoring using the ABCD2-score was determined and both hormones were measured on admission. The pri-

mary endpoint was a cerebrovascular re-event within 90 days. The secondary composite end point consisted of stroke, death, or presence of a high-risk stroke mechanism requiring specific early intervention (i.e. 50%> stenosis in the relevant vessel or a cardioembolic source).

Results: We included 107 consecutive TIA-patients. Re-events occurred in 10 patients (9%). The composite endpoint occurred in 33 patients (31%). Copeptin levels were higher in patients with a re-event compared to patients without re-event (p = 0.02). In patients fulfilling the combined endpoint (n = 33), copeptin levels were higher compared to patients without (p = 0.03). There was no difference in cortisol levels between these groups (p = 0.53, respectively p = 0.78). Copeptin revealed a higher area under the receiver-operating-characteristics curve (AUC) to predict re-events compared to the ABCD2 score (AUC of 0.73 versus 0.43; p <0.01). The combination of the clinical score and the biomarker showed an even higher overall prognostic accuracy with an AUC of 0.77(p = 0.002).

Conclusion: Measurement of plasma copeptin, but not cortisol levels in TIA-patients provides additional prognostic information beyond the ABCD2-clinical-risk-score alone. Routine Copeptin measurement could be an additional tool for risk-stratification after TIA.

FM 4 Late Whiplash – a Study comparing Randomized Treatments

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Background: To compare four different treatment strategies in patients suffering from chronic whiplash injury (symptoms persisting for more than 6 months after injury, Grade I or II, Quebec Task Force classification).

Methods: Patients fulfilling the inclusion criteria were randomly assigned to one of the following treatment groups: 1) local anesthetic infiltration, 2) physiotherapy, and 3) medication. Group allocation was stratified according to gender, age, and education. Additionally, patients of each treatment group were randomized 1:1 to cognitive behavioral therapy (CBT) or no CBT. Patients were assessed at baseline, after an 8 week treatment period, and then 3 and 6 months later, as follows: general physical and neurological examination, cervical spine MRI (at baseline), evaluation of psychosocial factors and litigation status (at baseline), subjective outcome rating (cured, improved, unchanged, worse), standardized pain assessment questionnaire (Mc Gill Pain Questionnaire), visual analogue scale (VAS), and self-assessment scores (well-being scale, self-rated cognitive ability, activities of daily living). Main outcome measures were: subjective outcome rating, pain intensity, and working ability.

Results: Of 91 enrolled patients 73 completed the study and 62% were women. After treatment (irrespective of the treatment group), 47 patients (64%) were subjectively improved (48%), or cured (16%), with a significant preponderance of women (73% versus 50%, p = 0.047). There was no difference regarding outcomes between the three treatment groups in men and women. The most robust difference was achieved with CBT, which was associated with a significantly higher rate of recovery (23% vs 9%), and improvement (53% vs 42%) (p = 0.024), and with a significant gender difference (p = 0.01), being more effective only in women (p = 0.004, men: p = 0.69). All treatments significantly improved pain intensity (VAS: p = 0.01, p = 0.003 and p = 0.000 and McGill total: p = 0.004, p = 0.122 and p = 0.014 for infiltration, medication and physiotherapy, respectively) without significant differences between the groups. Also, working ability improved overall (p = 0.023) in the infiltration and physiotherapy groups, but not in the medication group. CBT had a favorable influence independent of the primary treatment group (p = 0.003).

Conclusion: Intensive therapy in late whiplash syndrome can achieve improvement in two thirds of patients which is maintained beyond 6 months in half of them. Overall, women showed a higher rate of improvement. Additional CBT was the most effective treatment modality independent of the concomitant therapies, with a significant effect on outcome, including working capacity.

FM 5 Relapse of herpes simplex type 2 meningoencephalitis and progressive multifocal leukoencephalopathy in a patient treated with natalizumab for multiple sclerosis

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A now 41-year-old, male Caucasian patient experienced herpes simplex virus type 2 (HSV-2) meningoencephalitis in 2000. He recovered completely, but the MRI then also revealed T2 lesions suggestive of inflammatory disease as an incidental finding. In 2002, relapsing-remitting multiple sclerosis was diagnosed on the basis of three clinical relapses, progression of the MRI lesion load and oligoclonal bands in the cerebrospinal fluid (CSF) [1]. From 2003, he was treated with interferon-β1b, mitoxantrone (40 mg/m^2 body surface) and azathioprine, before monotherapy with natalizumab was begun in 2007 in the presence of normal blood cell counts. At this time, he had experienced 16 multiple sclerosis relapses in total, and the expanded disability status score (EDSS) was 3.5 [2]. During treatment with natalizumab, no further relapses occurred, the EDSS improved to 3.0, and the one-year follow-up MRI in 2008 showed a stable lesion load.

In May 2009, the patient developed fever and meningism. MRI showed a new T2-hyperintense lesion in the left occipital lobe (fig. 1a). CSF showed pleocytosis of 106 cells/µl, mostly lymphocytes, and no JC virus (JCV) DNA, but HSV-2 DNA (1037 copies/ml). HIV-screening was negative. A relapse of HSV-2 meningoencephalitis was suspected and treated with valaciclovir. Three weeks later, HSV-2 and JCV DNA were undetectable in the CSF, and control MRI showed no progression (fig. 1b). Natalizumab treatment was continued under valacyclovir prophylaxis (500 mg/day). In July 2009, follow-up MRI revealed a progression of the occipital lesion, which was asymptomatic except for increased light sensitivity (fig. 1c). Lumbar puncture revealed 7 cells/µl, no HSV-2 DNA, but of JCV in three laboratories (87–297 copies/ml), proving PML. Plasmapheresis was performed with three exchanges of the double plasma volume each, and mefloquine was initiated (250 mg at day 1, 2, 3, 8, and every 7th day thereafter) [3].

The CSF cell count and the detection of HSV-2 suggest that, in May, the patient had suffered a relapse of HSV-2 meningoencephalitis. However, the newly evolved lesion might already have been due to PML accompanied by a negative CSF result for JCV. It remains speculative whether HSV-2 meningoencephalitis or other conditions like the preceding immunosuppressive therapy might have disposed this individual to PML, which is a rare, but serious adverse event during natalizumab treatment [4, 5]. A history of viral meningoencephalitis may be considered as a contraindication for natalizumab treatment.

References

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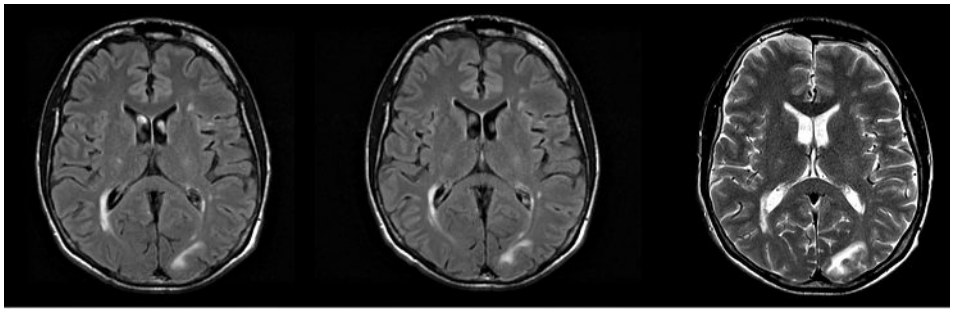
Figure

Axial MRI from 2009, 05/07 (1a, T2-FLAIR), 05/22 (1b, T2-FLAIR) and 07/22 (1c, T2; axial FLAIR not done).



1a 1b 1c

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FM 6 Parkinson's disease: adaptive gene expression changes in the healthy striatum

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Introduction: A unique feature of Parkinson›s disease (PD) is its asymmetry. In human, PD symptoms only appear after a very large striatal dopamine depletion. Several ipsilateral compensatory mechanisms could counteract dopamine denervation on the same side. However it is not yet known whether compensatory mechanisms of the less affected side could also play a role in the process. Our hypothesis in this study is that the healthy side of a unilateral PD rat model shows adaptive behaviorally important gene expression changes in direct and indirect pathways.

Methods: We analyzed the rat spontaneous locomotor behaviour four weeks after a unilateral 6-hydroxydopamine (6-OHDA) lesion and then studied the contralateral striatal expression of dynorphin (DYN) and D1 dopamine receptors (D1R) mRNA for the direct pathway and enkephalin and D2 dopamine receptors (D2R) mRNA for the indirect pathway. We also analyzed contralateral expression of several striatal and cortical glutamatergic markers, as well as nigral tyrosine hydroxylase (TH), to see whether contralateral changes in PD were due either to cortico- or nigrostriatal connections. The striatum was divided into two parts, medial (limbic) and lateral (motor).

Results: Mean velocity was decreased in 6-OHDA rats compared to other experimental groups, although not significantly. However, we found a positive and significant correlation between D1R mRNA expression in the lateral part of the contralateral healthy striatum and mean velocity both measured four weeks after surgery, in 6-OHDA rats only. Moreover we observed a significant increase in DYN and GAD mRNA in the lateral part of the contralateral parkinsonian striatum in absence of changes in other direct pathway genes. In contrast no contralateral changes were observed in the striatal indirect pathway neither with enkephalin nor with D2R gene expression. We also did not find any significant contralateral changes with TH, glutamatergic receptors or vGluT1.

Conclusion: Our results suggest a role of the striatal direct pathway on the healthy side to compensate the ipsilateral dopaminergic lesion and improve motor symptoms. This finding may be important to understand the course of PD in humans. The direct pathway could play a role in compensatory mechanisms of the less affected side slowing down the clinical progression of the disease.

Postersession, Freitag, 6.11.2009, 13.00–14.00 Uhr

Gruppe 1

01 A case report: Cerebral manifestation of non classifiable collagenosis

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A 65-year-old-woman was admitted to our hospital with acute focal neurological symptoms with left sided hemiparesis, hemianopsia to the right, dysarthria and an NIHSS of 13 points. In the ambulance during transfer to the hospital, focal epileptic seizures of the left arm were observed for the first time.

Perfusion-CT showed decreased perfusion in the territory of the right arteria cerebri posterior and part of the dorsal territory of the right arteria cerebri media. Native CT-scan showed no early signs of ischemia and bleeding, so the patient was administered intravenous thrombolysis. The focal neurological signs disappeared after thrombolysis, the NIHSS showed 0 points. Residual neurocognitive deficits with anosognosia, short term memory problems and disorientation were still present.

MRI-DWI showed no ischemia, only diffuse hyperintensity of the parietal lobe, the brainstem and the temporal lobe with normal ADC.

The status epilepticus could be interrupted by administering Lorazepam. Anticonvulsive treatment was started intravenously with Levetiracetam and changed to Carbamazepine.

Medical history showed a 6 month history of depression and B-symptoms with weight loss and inappetence.

Lab results showed pancytopenia, high CRP and increased erythrocyte sedimentation rate. Cerebrospinal fluid revealed pleocytosis with 13 cells/µl and elevated lactate (3.5 mmol/l) and protein (0.64 g/l) levels. Cytology, viral, bacterial and parasitic antibodies and PCR showed normal results. Paraneoplastic antibodies were absent.

Differential diagnosis of paraneoplastic syndrome or cerebral vasculitis/collagenosis led to further examinations. The mammography showed microcalcifications in both mammary glands, but biopsy showed no evidence of a malignant tumor; PET scan of the whole body was normal. In the clinical examination, livedo racemosa and diffuse subcutaneous oedema were noticeable. Skin biopsy attested typical changes attributed to lupus erythematosus but the vasculitis parameters, including testing for ANA and antiphospholipid-antibodies, were negative.

Considering a non classifiable collagenosis, we started a high dose steroid pulse therapy with 500 mg methylprednisolone per day for 5 days. The neurocognitive deficits declined.

Conclusion: Collagenosis should be considered in a patient with acute focal neurological deficit and additional symptoms, even if vasculitis parameters show negative results.

02 A subtype of Creutzfeldt-Jakob disease presenting with higher order visual disturbance including Balint syndrome

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Introduction: Creutzfeldt Jakob disease (CJD) is a prion disease typically presenting with progressive dementia accompanied by other neurological features such as cerebellar ataxia and myoclonus. In 1929, Heidenhain described a variant of the disease characterized by an initially predominating visual disorder and a rapid progression. We report the findings in a 64-years-old man admitted for investigation of progressive visual disturbances. Five months prior to admission, unspecific behaviour changes such as listlessness, insomnia, decline of interests and a slightly clumsy gait had started to develop and had been attributed to a possible episode of depression.

Results: Clinical evaluation at admission revealed a right-homonymous hemianopsia and a color vision disturbance. The patient presented difficulties in performing visual guided grasping (optic ataxia) and could not name the elements of the Poppelreuter figure (simultaneous agnosia). Identification of single objects, spontaneous grasping as well as coordination of non visual guided movements were intact. Tendon reflexes were increased on the left side.

Diffusion MRI demonstrated a gyriform signal predominantly in the left-parietooccipital cortex. The EEG revealed 1-2 Hz periodic theta/delta activity with recurrent sharp wave complexes (PSWCs) strongly left-lateralized in the

parietooccipital cortex. Cerebrospinal fluid contained increased levels of CSF 14-3-3 and S-100 protein.

Further neuropsychological evaluation was limited by a rapid progressive decline in visual and cognitive function culminating in cortical blindness. Later, myoclonus and ataxia emerged. The patient died 5 weeks after admission in a mutistic and blind state.

At autopsy the diagnosis of a spongiform encephalopathy was confirmed. Pathological structural changes including accumulation of proteinase-K resistant material were detected in both occipital cortices while frontal and temporal areas were relatively spared.

Conclusion: The Heidenhain variant of sporadic CJD may clinically develop from unspecific changes in comportment. Following thorough behavioural neurological assessment, the tentative diagnosis can be further consolidated by a combination of electrophysiological, neuroradiological and laboratory findings.

03 Acute crossed cerebellar diaschisis (CCD) as a network phenomenon in status epilepticus demonstrated by DWI

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Rationale: The term "diaschisis" refers to the phenomenon of transient/permanent loss of function in a brain region distant from the area of the cortical/subcortical primary brain lesion. Crossed cerebellar diaschisis (CCD) was observed in several supratentorial brain pathologies. CCD is rare in adults with chronic epilepsy; only two case reports deal with CCD after status epilepticus (SE). Diffusion weighted imaging (DWI) allows to detect acute tissue changes revealing energy metabolism compromise secondary to ictal activity. We report for the first time CCD findings during SE by means of DWI, although CCD was clinically not detectable because of non-convulsive SE (NCSE).

Case: A 74-year-old woman was found unresponsive and she had a generalized-tonic-clonic seizure on emergency admission. Examination revealed unresponsiveness and right, but not left, arm movements to painful stimuli. She had fixed left-upward gaze and right-sided pupillary dilatation. She was transferred to the intensive care unit for monitoring and therapy

Results: Her EEG showed right-hemispheric focal NCSE (fig. 1). CSF was normal. MRI revealed widespread cortical DWI hyperintensities and corresponding apparent diffusion coefficient (ADC) reductions in the right hemisphere including thalamus, hippocampus, head of the caudate, and parts of the occipital areas together with pronounced cortical swelling of affected areas. This pattern of DWI abnormality and normal MR-angiography excluded brain ischemia. Contralaterally, the left cerebellar hemisphere too showed DWI hyperintensities and reduced ADC although less marked (fig. 2).

NCSE was refractory to extensive anti-convulsive therapy. The patient died 4 days later from multi-organ failure.

Conclusions: SE may damage the brain by excitotoxicity resulting from glutamate spillover and an increase of intracellular calcium. Membrane peroxidation and energy exhaustion with breakdown of electrolyte and water homeostasis eventually lead to acute cell death. These mechanisms may be visualised by MRI, especially by means of DWI which may show laminar cortical cytotoxic swelling. Proposed mechanisms of CCD were glutamatergic propagation of hyperexcitation through the corticopontocerebellar tracts and/or GABAergic disinhibition of these tracts after lesions of the controlling inhibitory interneurons. Our findings based on imaging techniques like DWI may help to visualize the pathophysiological and neuroanatomical understanding of CCD during SE.

Figure 1

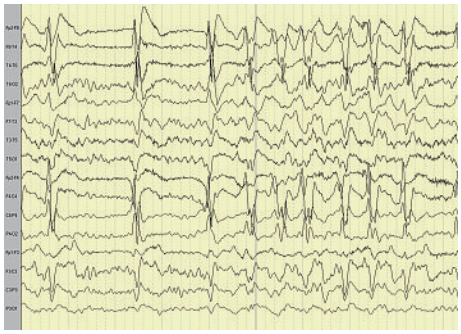
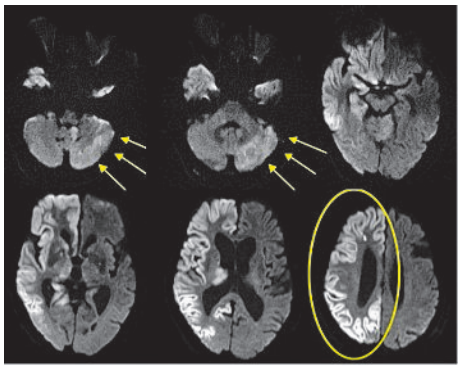


Figure 2



04 APO010, a synthetic hexameric CD95 ligand, induces human glioma cell death in vitro and in vivo

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Introduction: Death receptor targeting has emerged as one of the promising novel approaches of cancer therapy. The activation of one such prototypic death receptor, CD95 (Fas/APO-1), has remained controversial because CD95 agonistic molecules have exhibited either too strong toxicity or too little activity. The natural CD95 ligand (CD95L) is a cytokine which needs to trimerize to mediate a cell death signal. Mega-Fas-Ligand, now referred to as APO010, is a synthetic hexameric CD95 agonist that exhibits strong antitumor activity in various tumor models.

Methods: The cytolytic activity of APO010 was assessed by crystal violet assays in the glioma cell lines LNT-229, U87MG and LN-308. Induction of apoptosis in these cell lines and 9 primary glioblastoma cell cultures from freshly resected human tumors was quantified by staining with annexin V and flow cytometry. The activation of caspases 8 and 3 and cleavage of PARP was assessed by immunoblot. The activation of caspase 3 was assessed additionally by DEVD-amc cleavage assay. LNT-229 cells were co-treated with temozolomide and APO010, the fraction of surviving cells was assessed following annexin V staining and flow cytometry. Synergy of temozolomide and APO010 was calculated using the fractional product method. For in vivo experiments, 100.000 U87MG cells were implanted orthotopically in the right striatum of nude mice. Locoregional treatment with APO010 was performed on days 7 and 14 after tumor inoculation. Systemic treatment was performed on three days per week by intraperitoneal injection of APO010 until the mice had to be sacrificed. Histologic analysis included H&E and TUNEL staining and immunohistochemical assessment of cleaved caspase 3.

Results: Here, we studied the effects of APO010 in human glioma models in vitro and in vivo. Compared with a cross-linked soluble CD95L or a CD95-agonistic antibody, APO010 exhibited superior activity in glioma cell lines expressing CD95 and triggered caspase-dependent cell death. APO010 reduced glioma cell viability in synergy when combined with temozolomide (TMZ). The locoregional but not the systemic administration of APO010 induced glioma cell death in vivo and prolonged the survival of tumor-bearing mice by induction of apoptosis on tumor cells but not in normal brain.

Conclusion: A further exploration of APO010 as novel anti-glioma agent is warranted.

05 Autoimmune myasthenia gravis after sternal fracture

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Clinical case: We report a 54-year-old woman who developed blurry vision two months after suffering a sternal fracture due to a car accident. Thereafter, she complained fluctuating generalized weakness. Five years later, the diagnosis of myasthenia gravis made by detection of significant concentrations of acetylcholine receptor antibodies in the blood, and the patient came to our hospital. Treatment with pyridostigmine normalized the muscular strength.

Discussion: Speculatively, the damage of atrophic thymic remnants due to a sternal fracture might induce an autoimmune response to thymic acetylcholine receptor molecules or might increase an existing subclinical antibody

response. Similar mechanisms have been proposed for the occurrence of autoimmune myasthenia gravis after cardiac surgery. The knowledge about such putative associations may be helpful for diagnostic procedures and may be relevant from a medicolegal perspective.

06 Cervical muscle area measurements in whiplash patients – acute, 3 and 6 months follow-up

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Introduction: The role of the cervical spine muscles in whiplash injury is disputed. We hypothesized to find cervical muscle atrophy in the long-term, probably related to pain or inactivity.

Methods: 90 symptomatic patients (48 females) were recruited from our emergency department and examined within 48 hours, and 3, and 6 months after a motor vehicle accident. MRI cross-sectional muscle area (CSA) measurements were performed bilaterally of the cervical extensor muscles using axial STIR (Short Tau inversion Recovery) sequences on level C2 (deep and total dorsal cervical extensor muscles), C4 (sternocleidomastoid muscles) and C5 (deep and total dorsal cervical extensor muscles) using Picture Archiving and Communication System (PACS). Two blinded trained raters independently performed the measurements. CSAs were correlated with clinical outcomes (EuroQuol, Whiplash Disability Score, neck pain intensity [VAS], cervical spine mobility).

Results: There was a high agreement between the two raters (intra class correlation: 0.815–0.980). There were no significant changes of muscle CSAs at the three levels over time. Women consistently had smaller CSAs than men. There were no consistent significant correlations of CSA values with the clinical scores at all time points except with the BMI.

Conclusion: Our results do not support a major role of cervical muscles in the genesis of symptoms after whiplash injury.

07 Comparative judgement of time: the impact of spatial neglect and caloric stimulation

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Temporal information has become an important element for the majority of people in the 21st century. Recent observations indicated that cultures with a left-to-right written language map the past to the left side of space and the future to the right (Santiago et al., 2007). In contrast to patients with neglect, healthy individuals show a perceptual bias towards the left side ("Pseudoneglect"; Bowers & Heilman, 1980), which also exists for the processing of time. In particular, the first presentation of two light-flashes with identical durations is typically perceived longer (Rose et al., 1995). The present study investigated temporal information processing in patients with neglect. In addition, we manipulated the processing of time in healthy observers by applying caloric stimulation, which has been shown to produce a rightward shift in the sense of neglect-like behaviour (Karnath et al., 2003).

A train of three identical auditory stimuli, separated by intervals of different lengths, was delivered to patients with neglect as well as healthy participants. Intervals were of the following durations (first/second; in msec): 1) 1500/1500, 2) 1400/1600, 3) 1300/1700, 4) 1200/1800, 5) 1600/1400, 6) 1700/1300, 7) 1800/1200. Participants were required to perform a comparative judgement of the interval durations. The healthy participants were tested under caloric stimulation, for which warm (44 °C) or cold (30 °C) water was injected in the left and right auditory canal.

Unlike healthy individuals, the patients with neglect showed a preference to perceive the second interval longer than the first one. In accord, neglect-like behaviour could be produced under bithermal caloric stimulation of the right but not the left ear in the healthy participants.

The present findings indicate a spatio-temporal interaction for comparative judgements of temporal information in patients with neglect and healthy individuals. In accord with earlier work, they strengthen the notion of a general magnitude system (Walsh, 2003; Conson et al., 2008) and support the idea of a common neural basis for the representation of space, quantity and time in the parietal lobes (Hubbard et al., 2005).

08 Differential localization of RhoGTPases after focal cerebral ischemia in rats

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Background/aim: Small GTPases of the Rho family, such as Rac1 and Cdc42, are key regulators of actin cytoskeleton that have been known to mediate cell death after ischemic stroke. The goal of this study was to determine changes in localisation of Rac1 and Cdc42 in the rat brain after ischemia.

Methods: Transient focal ischemia was induced by occluding the middle cerebral artery for 90 minutes (damage mainly in the striatum). Rats were sacrificed 24h after reperfusion and brains were used for immunohistochemistry analysis. Double immunostaining of Rac1 and Cdc42 with TUNEL (apoptotic cells) and a neuronal marker NeuN was used to identify the cellular localization in the ischemic side.

Results: Rac1 was upregulated in the peri-infarct region. Co-immunostaining studies showed that Rac1+ve cells were also TUNEL+ve and NeuN+ve. Expression of Rac1 in core area of infarct was not observed. Cdc42 was slightly reduced in the ischemic region, and only a small group of Cdc42+ve cells were TUNEL+ve. In addition, most of the Cdc42+ve cells were not labelled with NeuN.

Conclusion: These results suggest that Rac1 and Cdc42 may play differential role in ischemia-related apoptotic pathway.

09 Epic dreaming: clinical and polysomnographic findings in three patients

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Introduction: Epic dreaming (ED) is a disorder of unknown origin that has been reported in two full-length articles and two abstracts. It is characterized by dreams that are experienced as excessive and continuous throughout the night, resulting in daytime fatigue. We report the clinical and polysomnographic features of three patients with ED.

Methods: Three patients with ED were identified out of over 1000 consecutive patients seen in our outpatient sleep clinic. Assessment included a detailed neurological examination and polysomnography (PSG).

Results: Patient 1: A 20-year-old woman reported a three-year history of excessive neutral-content dreaming. Dreams had long, complicated plots and involved multiple dream characters that she could interpret from different perspectives. Patient 2: A-24-year-old woman had been experiencing exhausting nightmares for two years, in which she would witness violent scenes, such stabbing or fighting, as an observer. Patient 3: A 69-year-old man related a 5-year history of excessive dreaming involving his past activity as a cook, in which he would mentally rehearse the sequence of steps involved in the preparation of a meal.

Patients 1 and 2 had a history of depression and cardiac arrhythmias, while patient 3 was known for recurrent vertigo, essential tremor and prostate cancer. Neurological examination was normal in patient 1, revealed attention deficits in patient 2 and short term memory loss in patient 3. PSG documented sleep fragmentation

in patients 2 and 3 (due to bruxism and PMLS respectively). All patients had persistent epic dreaming on follow up interviews after 0.5–2 years.

Conclusion: ED appears to be a heterogenous disorder, in which sleep fragmentation might play a major role. Our observations support the existence of at least two subtypes, including "story epic dreaming" and "non-story epic dreaming".

10 Evolution of sleep spindles after paramedian thalamic stroke

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Introduction: Thalamus is a key structure in the generation of sleep spindles. Sleep spindles have been associated with cognition and learning. Recovery in sleep spindles after hemispheric stroke has been reported and a role in plastic recovery changes has been suggested. We aimed at investigating the evolution of sleep spindles after paramedian thalamic stroke and at comparing them to healthy controls.

Patients and methods: Eight patients, two with bilateral paramedian thalamic stroke (PMTS) and six with unilateral PMTS and six age and gender matched controls underwent high-density EEG (hd-EEG) examination with 128 electrodes during sleep. Seven patients were studied twice and six patients three times: in the acute phase after stroke, 3 and 6 months later. Sleep spindles power was averaged over all electrodes and analyzed as previously reported.

Results: There were two patients, one with unilateral and one with bilateral PMTS with no peak in the spindle frequency range. The patient with bilateral PMTS was studied three times and in none of the tests a spindle peak was detected. In all control subjects a spindle peak was detected. Repeated measures ANOVA showed no difference in the patients group over time ($p = 0.65$, $F2 = 0.303$). T-tests showed no difference in the spindle peak power between patients and control subjects either.

Conclusion: Sleep spindles, if decreased, do not recover after PMTS. Complete loss of sleep spindles was observed only in two patients with PMTS, one with unilateral and one with bilateral lesions. This suggests that a unilateral thalamic lesion is enough for the complete loss of sleep spindles, depending on its specific location.

Support: The study is supported by the Zurich Center for Integrative Human Physiology (ZIHP).

Postersession, Freitag, 6.11.2009, 13.00–14.00 Uhr

Gruppe 2

11 Hemispheric lateralization of the corticostriatal glutamatergic system in the rat

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Introduction: Inhibitory gamma-aminobutyric acid (GABA)-ergic medium spiny projection neurons in the striatum receive glutamatergic afferents from the cortex. N-methyl-D-aspartate (NMDA) receptors are implicated in many neurological disorders, including Parkinson's disease (PD). Recently, we described a specific lateralization of the striatal direct pathway, with a predominance of the left striatum, related to non-motor function. The hypothesis of the present study is that the lateralization of striatal direct pathway is due to a lateralization of glutamatergic corticostriatal projection.

Methods: In healthy rats, we investigated the striatal gene expression of three different NMDA receptors subunits (NR1, NR2A and NR2B). We also analyzed the vesicular glutamate transporter 1 (vGluT1), a presynaptic component of the corticostriatal projection in the limbic cingulate cortex (Cg), the medial agranular cortex (AGm), an association premotor cortex, and the primary motor cortex (M1).

Results: We found a significantly higher expression of NR2A mRNA in the medial sector of the left striatum. No difference between the right and left striatum was detected either with NR1 or NR2B mRNA. In the cingulate cortex, vGluT1 mRNA expression was also higher in the left hemisphere. We did not observe any side difference neither in AGm nor in M1.

Conclusion: Our study demonstrates a lateralization of both the striatal glutamatergic receptors and the cortical presynaptic glutamatergic system, probably related to limbic function, with a predominance on the left side. We suggest that this lateralization concerns the direct pathway. Lateralization of the corticostriatal projection of the direct pathway could be implicated in the pathophysiology of asymmetric diseases like PD. Further studies are required to relate this finding to behaviour.

12 Homocysteine alters the effects of Zinc and Copper on recombinant amyloid-beta peptide aggregation

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Homocysteine (Hcy) is a nonessential amino acid formed as an intermediate during the metabolism of methionine to cysteine. Hyperhomocysteinemia has been associated with various neurological disorders including Alzheimer's disease (AD). One central phenomenon of AD is the formation of amyloid plaques. These plaques are composed of fibrillar amyloid-beta peptides (Abeta peptides), other proteins and transition metal ions like Zn(II) and Cu(II). Levels of extracellular zinc and copper are normally low.

The impact of homocysteine, zinc and copper on Abeta peptide aggregation was analyzed using a microtiter plate-based Thioflavin T aggregation assay.

The presence of Hcy did not relevantly change the aggregation behaviour of Abeta peptides. When observed in the absence of Hcy, the transition metals Zn(II) and Cu(II) inhibited the aggregation of Abeta peptides. Co-incubation with Hcy reduced the effects of Zn(II) and Cu(II). This effect depended on the molar ratio between metal ions and Hcy. With Hcy concentrations corresponding to pathophysiologically occurring hyperhomocysteinemia, Zn(II) and Cu(II) in physiological concentrations were no longer able to reverse aggregation behaviour. Other ions studied (Na, K, Ca, Fe, Mg) did not change Abeta peptide aggregation.

By binding Zn(II) and Cu(II), Hcy can promote the formation of Abeta peptide fibrils. This observation may be an explanation of the association between hyperhomocysteinemia and AD.

13 Imaging blood-brain barrier transporters in low-grade glioma patients with positron emission tomography, tyrosine and choline

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Introduction: Amino acids are actively transported across the blood-brain barrier (BBB). Increased transport in low-grade gliomas (LGG, WHO II) gives rise to detect these tumors with positron emission tomography (PET) and amino acid analogues, e.g. F18-fluoro-ethyl-tyrosine (FET). In a clinical setting FET PET may be applied to define targets for stereotactic biopsy, and for follow-up of LGG during treatment. However, up to 20% of LGG are FET-negative. Here we assessed whether FET-negative tumors can be visualized with PET and radiolabeled choline. Choline is involved in intracellular signalling associated with proliferation, and is incorporated into membrane lipids of dividing cells.

Methods: We analyzed the uptake of F18-fluoro-choline (CHO) in six patients with FET-negative LGG (three fibrillary astrocytomas, three oligodendroglial tumors, age 42–60 yr). The diagnosis of LGG was confirmed histopathologically in all patients. None of the tumors showed gadolinium enhancement on MR. Uptake of FET and CHO was quantified by normalizing the tumor tracer uptake to the mean of the cerebellar uptake. Values >1.0 indicate increased transport relative to the normal brain.

Results: The mean FET tumor uptake was 0.95 (range 0.91–1.00). By visual inspection

none of the six tumors showed increased CHO uptake. In accordance the mean CHO tumor uptake was 0.89 (0.73–1.15).

Conclusions: In this series imaging with CHO was not superior to FET in detecting LGG. Our data indicate that a subset of LGG has a very low metabolic demand for both substrates, and suggest that neither amino acid nor choline pathways are significantly upregulated independently.

14 Impaired digital dexterity in Parkinson's disease is associated with higher-order praxis function

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Background: A controversial concept suggests that impaired digital dexterity in PD may be explained by limb kinetic apraxia (LKA) as it is little responsive to dopaminergic treatment. The goal of the present study was to explore the relationship of digital dexterity (as measured by coin rotation, CR) with praxis function (assessed by the test of upper limb apraxia, TULIA) and parkinsonian symptoms (MDS-UPDRS).

Methods: Ten PD patients (3 women, mean age 63.4) with wearing off fluctuations were assessed on both arms separately. Testing was done in OFF and ON state as defined by MDS-UPDRS (average decrease of scores 66%). In the CR task patients were requested to rotate a 50 Rappen coin as fast as possible between their thumb, index and middle finger. CR performance was analyzed by measuring the frequency during three 10 second periods. Gesture production was assessed by the TULIA, balanced for predominant finger and hand postures. Both CR and TULIA were assessed by a blinded rater based on video recordings. Within-subject analyses were done by Pearson's correlation between summed scores of measurements and by paired t-tests for comparisons between OFF and ON state.

Results: CR scores significantly correlated with TULIA scores ($r = 0.63$ $p = 0.05$) and not with MDS-UPDRS ($r = –0.32$ $p = 0.37$), irrespective of the motor state, although only 4 patients scored slightly below the cut off for apraxia. The correlation of CR and TULIA scores was even stronger, if considered in OFF only ($r = 0.77$ $p = 0.01$). CR and finger gestures did not change between OFF and ON state ($p = 0.56$ and $p = 0.35$, respectively), while hand gestures improved in ON ($p < 0.001$).

Conclusions: The significant association of CR with TULIA but not MDS-UPDRS indicates that impaired dexterity in PD may be indeed apraxic rather than bradykinetic in nature. Furthermore, digital dexterity did not improve with dopaminergic treatment supporting the notion of LKA underlying dexterous difficulties in PD.

15 Is lymphocytosis a predictor for good response to Natalizumab treatment in Multiple Sclerosis?

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Introduction: Treatment with Natalizumab (Nb), a monoclonal antibody blocking the migration of T and B cells into the CNS, leads to an elevation of lymphocytes, monocytes, eosinophiles and basophiles in peripheral blood in many patients. The mechanisms underlying these findings are not completely understood, but several hypotheses exist: It's thought to be a sequestration in peripheral blood by inhibition of migration into the tissue, a reaction to latent virus activation or even a particular Nb induced activation. We analyzed if a lymphocytosis (LS) has a predictive value for a good response to Nb in patients with Multiple Sclerosis (MS).

Methods: This is a retrospective study. Inclusion criteria were treatment with Nb for at least one year, two differential blood examinations under treatment and a baseline and follow up MRI after one year. We statistically analyzed the sensitivity, specificity, positive predictive value and negative predictive value for good response to Nb using the parameters absolute LS, relative LS and relative granulocyte count <50% separate and in combination.

Results: We will present preliminary results. The interpretation of our findings is hampered by a small sample size and difficulties to establish reliable criteria for insufficient response in Nb treated patients.

Conclusion: It is desirable to have reliable laboratory markers for insufficient response to Nb treatment in MS patients. LS probably is such a reliable marker. To clarify this issue further studies with higher sample size are needed.

16 Multifocal reversible MRI Abnormalities in prolonged Status epilepticus

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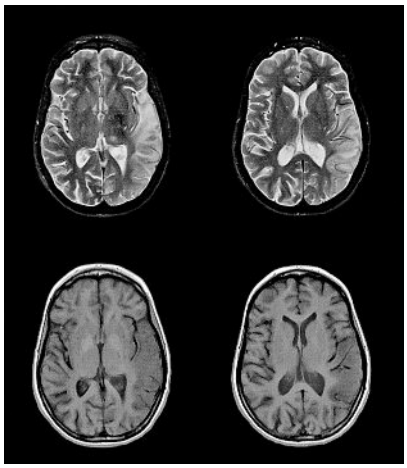
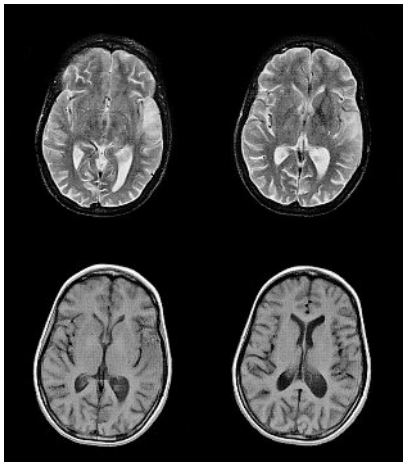
Introduction: Refractory status epilepticus is a devastating disorder leading to variable damage of the brain. Various patterns of MRI abnormalities have been reported but there are quite few follow up investigations published.

Methods: Single patient MRI series and case report.

Results: A 20-year-old woman presented to our department after two generalized epileptic seizures. MRI showed left temporal T2 hyperintense and T1 hypointense abnormalities (Image 1).

After therapy with levetiracetam. the patient initially recovered. Ten days later the patient developed fluctuating aphasia, somnolence and vomitus and the diagnosis of non-convulsive status epilepticus was confirmed by electroencephalography (EEG). Follow-up MRI demonstrated a profound increase of abnormalities (image 2) which were partially ameliorated 2½ weeks later after antiepileptic therapy with levetiracetam, phenytoin, topiramate and pregabalin. The patient remained seizure-free and EEG normalized.





Follow-up MRI three months showed a further resolution of abnormalities but remaining tissue damage.

Etiology of seizures remained unclear. The patient had mild preexisting cognitive impairment. There was no evidence of encephalitis, meningitis, vasculitis or brain tumor.

Conclusions: Prolonged status epilepticus can cause pronounced damage in involved brain structures. Corresponding abnormalities in imaging are variable. Our patient showed widespread abnormalities of MRI imaging and a very striking reversibility of most changes.

Further systematic studies are needed for a better understanding of pathogenetic and prognostic relevance of these findings

17 Olfactory function in patients with dopamine and/or hypocretin deficit and in patients with excessive daytime sleepiness

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Introduction: Hyposmia is common in patients with Parkinson's disease (PD). Olfactory deficits were recently reported also in patients with narcolepsy and linked to hypocretin deficit/neuronal degen-

eration. The role of daytime sleepiness, dopamine and hypocretin on olfactory function is poorly known.

Aim: to examine olfactory function in patients with narcolepsy, restless legs syndrome (RLS), PD, excessive daytime sleepiness (EDS) and healthy controls.

Patients and methods: We studied 14 patients with PD, 11 patients with narcolepsy, 10 patients with RLS, 8 patients with EDS and 15 controls. Olfactory threshold, discrimination and identification were assessed using standardized "Sniffin' sticks" test. Sleepiness was assessed using Epworth sleepiness scale (ESS), Karolinska (KSS) and Stanford sleepiness scale (SSS).

Results: One-way ANOVA showed a significant difference between groups for threshold ($p<0.001$, $F4=7.1$), discrimination ($p<0.001$, $F4=13.5$) and identification ($p<0.001$, $F4=16.2$). Post-hoc t-tests revealed that patients with PD performed significantly worse for all three olfactory parameters than all other groups. Only for threshold PD patients were not significantly different from patients with EDS ($p = 0.066$). Olfactory functions were similar in patients with narcolepsy, EDS, RLS when compared to healthy controls.

Conclusion: We confirm the presence of olfactory deficits in PD but not in narcolepsy, who as patients with RLS and EDS- performed similarly to healthy controls.

18 On the interaction of homocysteine metabolism and Alzheimer's disease: in vitro and in vivo experiments

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Sporadic Alzheimer's disease (AD) is the most common cause of dementia. Increased homocysteine (Hcy) plasma and CSF levels are a risk factor for AD. Although the association between hyperhomocysteinemia and AD is well established, the underlying pathophysiology is unexplained. In particular, it is not known whether Hcy itself or other components of the homocysteine metabolism, e.g., S-adenosylmethionine (SAM), folate or vitamin B12, play a role in the development of AD. The objective of this study was to define the major player of Hcy metabolism in respect to relevance for AD.

We manipulated different parts of Hcy metabolism in human embryonic kidney (HEK) cell lines by adding Hcy or SAM to the cell culture media and by dietary changes in transgenic mice over-expressing the amyloid-precursor protein (APP) and analyzed AD-specific parameters e.g., APP-processing, gene expression patterns and markers of oxidative stress. Our cell culture results suggested that Hcy influences processing and expression of APP in HEK cells, i.e., in a dose-dependent manner, Hcy concentrations of 1, 2.5, 5 and 10 mM, 4 h incubation, lead to a significant decrease of both C-terminal APP fragments.

In addition, Hcy incubation led to a reduction of oxidized glutathione of more than 50 % of the control value while it did not influence the levels of total glutathione. This effect was seen in transfected as well as in wildtype HEK cells.

There are many candidates for speculative interactions between Hcy metabolism and AD pathogenesis. Our results support the hypothesis that Hcy leads to an up-regulation of gamma-secretase activity. However, effects of Hcy on the redox system may further contribute to an influence of Hcy on neurodegeneration.

19 Parkinson's disease and Alzheimer's dementia in patients with narcolepsy

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Background: The etiology of narcolepsy is unknown. An autoimmune but also a neurodegenerative process involving the hypocretin (orexin) neurons of the hypothalamus are currently discussed. Hypocretin deficiency is known to occur in Parkinson's disease (PD) and other neurodegenerative disorders.

Aim: To report two patients with a long history of narcolepsy with cataplexy, in which Parkinson Disease (PD) and Alzheimer's dementia (AD) subsequently developed.

Patients and methods: Two male patients underwent an assessment which comprised a clinical and neurological evaluation with detailed sleep history; both patients received the diagnosis of narcolepsy on clinical and laboratory basis (CSF Hypocretin-1 levels, PSG/MSLT investigations).

Results: The first patient, a 67-year-old male, suffers from narcolepsy with cataplexy since the age of 17. He has a typical clinical narcoleptic tetrade and typical neurophysiological findings. The HLA typing is positive (HLA DQB1*0602) the and CSF hypocretin-1 is undetectable. At the age of 60 he developed resting tremor, micrographia and right bradykinesia; the brain MRI was normal. The motor symptoms responded to L-DOPA and the diagnosis of PD was made. Narcoleptic symptoms, especially cataplexia, also improved with L-DOPA treatment.

The second patient, a 69-year-old male, suffers from narcolepsy with cataplexy since adolescence. The diagnosis was made only at the age of 62. He has a typical clinical narcoleptic tetrade and typical neurophysiological findings. The HLA typing is positive (HLA DQB1*0602) the and CSF hypocretin-1 is undetectable. At the age of 65 he presented early signs of dementia, characterized by spatial disorientation, short term memory deficit, reduced attention and reduced verbal fluency. Brain MRI evidenced diffused cortical atrophy without focal lesions. The diagnosis of Alzheimer disease, probably familiar type (his mother had the same clinical picture) was made. As AD progressed (his actual MMSE score is 20/30) paraphasias and neologisms appeared.

Conclusion: The association between narcolepsy, PD and AD has not been reported in the literature and while probably fortuitous suggests a need for systematic study on the long term evolution of patients with hypocretin-deficient narcolepsy.

20 Psychopathologische Befunde bei Patienten mit idiopathischem Restless-legs-Syndrom

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Hintergrund: Das Restless-legs-Syndrom (RLS) ist eine häufige neurologische Erkrankung, die oftmals mit psychischen Störungen assoziiert ist. Ergebnisse aus Studien belegen ein überdurchschnittlich häufiges gemeinsames Auftreten von RLS und Angst- und depressiven Störungen, aber auch somatoformen Störungen sowie eine Aufmerksamkeits-/Hyperaktivitätsstörung (ADHS).

Ziel: Ziel der Studie war es, psychopathologische Befunde auf Symptom- sowie Diagnoseebene bei RLS-Patienten aufzuzeigen. Der Fokus liegt dabei auf den Störungsbildern der depressiven, Angst-, und somatoformen Störungen sowie der ADHS.

Methoden: 49 Patienten mit der Diagnose eines idiopathischen RLS wurden prospektiv mittels des diagnostischen Expertensystems DIA-X bezüglich der Häufigkeit psychischer Störungen in den letzten 12 Monaten befragt sowie anhand diverser Fragebogen zur psychischen und physischen Befindlichkeit untersucht.

Ergebnisse: Die Resultate des diagnostischen Expertensystems DIA-X ergaben auf Störungsgruppenebene bei insgesamt 18,3% der untersuchten RLS-Patienten eine somatoforme Störung, bei 16,3% eine depressive Störung, bei 12,2% eine Angststörung, bei 4,1% eine posttraumatische Belastungsstörung sowie bei 2,0% eine Essstörung. Es zeigten sich keine signifikanten soziodemographischen Unterschiede zwischen Probanden mit psychischen Störungen und Probanden ohne psychische Störungen.

RLS-Patienten mit auffälligen depressiven Symptomen (gemäss HADS-D/D) zeigten ein signifikant schwereres RLS, eine höhere Erschöpfung sowie eine grössere psychische Beeinträchtigung der Lebensqualität. Dieser Gruppenunterschied konnte bei Probanden mit Angstsymptomen (gemäss HADS-D/A) nicht festgestellt werden.

Schlussfolgerung: Psychische Störungen, insbesondere Depression, Angst- und somatoforme Störungen sind eine häufige Ko-Morbidität bei RLS und sollten vermehrt bei der Diagnostik und Therapie der Erkrankung berücksichtigt werden.

Postersession,
Freitag, 6.11.2009, 13.00–14.00 Uhr

Gruppe 2

21 Recurrent tumefactive demyelination without evidence for multiple sclerosis or brain tumor

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Introduction: The differential diagnosis of single space occupying lesions comprises multiple sclerosis (MS) in younger patients, and primary or secondary brain tumor at any age. We present a 70-year-old man with recurrent tumefactive demyelination (TD), which is considered to result from demyelination. Some authors suggest that TD may evolve into MS or primary CNS lymphoma.

Methods: This patient developed four single tumor-like, gadolinium enhancing lesions at different sites of the brain over three years. There was no preceding viral infection or vaccination. From the initial appearance on MRI CNS lymphoma was suggested. However, biopsy at first presentation revealed perivascular lymphocytic cuffs and macrophages. Over two years three CSF analyses showed mild lymphocytic pleocytosis, elevated protein, but no oligoclonal bands. FDG PET was negative at two, and positive at one manifestation. 14 months after onset of TD the patient also developed myelodysplastic syndrome (MDS) with isolated genomic deletion of 5q-. In addition renal cancer was diagnosed 11 months later.

Results: All cerebral lesions responded within 2 to 3 months to dexamethasone. The patient died after 33 months due to metastatic renal cancer. The final histopathological diagnosis obtained from autopsy of the brain was identical to the initial diagnosis from the biopsy. No tissue changes consistent with brain tumor – in particular lymphoma – were found.

Conclusions: Age, clinical course with recurrent single lesions and negative oligoclonal bands suggest that TD must be considered differently from MS. A relationship between TD and MDS or malignant cancer in our patient remains speculative but may have an immunological dysbalance as cause. Treatment other than steroids is not established for TD.

22 Remembering negative events induces leftward deviation in a line bisection task

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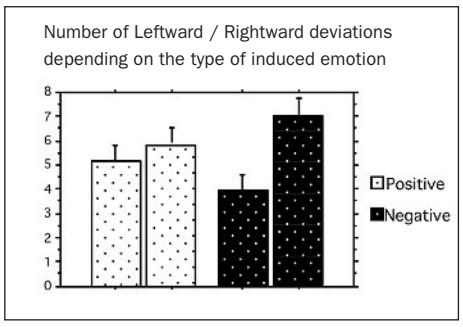
Introduction: Previous studies suggest a relation between emotion and spatial attention. More specifically, personality traits like optimism or positive mood were found to be associated with a rightward orientation preference (Drake, 1992; Gasper, 2002). In this study, we investigated whether inducing positive or negative emotions while bisecting lines may have opposite effects on the direction of participants' displacements.

Methods: Participants (40 healthy right-handed adults) were required to mark the midpoint of each of 24 horizontal lines (line length 26 cm) with a sharp pencil held in the dominant right hand (one line per sheet). While executing this task, subjects were asked to try to remember and contemplate once a positive (during 12 lines) and once a negative autobiographical event (during 12 lines; order of emotion counterbalanced). The number of leftward vs rightward deviations were recorded in each run, and an average deviation from the midline over all 24 lines was obtained for each participant, again for each run.

Results: ANOVA of the number of leftward vs rightward displacements with induced emotion (positive or negative) as the repeated measure revealed significantly more leftward displacement under negative emotion, and no systematic directional bias under positive emotion (see figure).

Conclusion: Over both emotion conditions, there were more left-sided than right-sided displacements ("pseudoneglect"). This result confirms previous findings of a leftward bias in normal participants when bisecting horizontal lines (Jewell, 2000). Pseudoneglect was significant only for the run during which subjects contemplated the negative autobiographical event. This observation is in line with "valence theories" of emotional hemispheric processing, which postulate a right hemisphere mediation of negative emotions. The reason(s) why positive emotions could not overcome pseudoneglect remain to be elucidated in future research.

Figure



23 Remission of an anti-MuSK positive seronegative Myasthenia gravis under Rituximab therapy

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Introduction: It is well known that patients with anti-MuSK positive seronegative Myasthenia gravis often do not respond sufficently to a therapy with inhibitors of cholinesterase and immunosuppressive therapy. Remission under intravenous immunoglobuline (IVIG) therapy is often only of short duration.

Methods: Case study of a single female patient with myasthenia gravis case.

Results: We report a female patient, who presented for the first time with bulbar symptoms at our hospital at the age of 43 years (2005). The diagnosis of an anti-MuSK positive seronegative Myasthenia gravis was made and therapy with low dose steroids and azathioprin initiated. Under IVIG therapy the patient improved to a remission. During the following years the disease generalised with recurrent neurological impairments, severe loss of weight and dyspnea, despite accompanying therapy with inhibitors of cholinesterase, azathioprin and low dose steroids and repeated cycles of IVIG.

The clinical course was complicated by multiple embolic events that led to the diagnosis of an antiphospholipid antibody syndrome.

So therapy was switched to Rituximab. A first cycle was given in 10/2008 under which remission could be achieved. A consolidating cycle was given in 5/2009 and the patient is still in remission. The accompanying immunosuppressive therapy as well as the therapy with cholinesterase inhibitor could be tapered.

Conclusion: Our patient responds well to the treatment with Rituximab. Therefore a therapy with Rituximab should be considered in patients, who appear to be refractory to a therapy under other immunosuppressive therapy.

24 Restless-legs-Syndrom (RLS) oder «RLS-like»? – Psychobiologische Untersuchungen bei Patienten mit idiopathischem RLS

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Hintergrund: Die Diagnose Restless-legs-Syndrom (RLS) wird primär anhand klinischer Diagnosekriterien gestellt. Supportive Kriterien wie das Auftreten von periodischen Beinbewegungen im Schlaf («PLMS») unterstützen die Diagnose. Bei RLS-Patienten besteht oftmals eine psychiatrische Ko-Morbidität. Einzelne Studie weisen für diese Gruppe von RLS-Patienten auf starke Ausprägungen bezüglich subjektiv eingeschätzter Variablen (Schweregrad des RLS, Müdigkeit, Beeinträchtigung der Lebensqualität, Somatisierungstendenzen) und schwache Ausprägungen bezüglich objektiv messbarer Variablen (z.B. PLMS) hin («RLS-like«).

Ziel: Ziel der Studie war es, RLS-Patienten ohne und mit psychischen Störungen hinsichtlich der unterschiedlichen Ausprägungen psychobiologischer Faktoren zu untersuchen.

Methoden: In dieser prospektiven Studie wurden 49 «de novo»-Patienten mit der Diagnose eines idiopathischen RLS mit dem diagnostischem Expertensystem DIA-X in die Gruppen «ohne psychische Störungen» (N = 30) und «mit psychischen Störungen» (N = 19) kategorisiert.

Der Vergleich der beiden Gruppen bezüglich psychobiologischer Faktoren erfolgte anhand verschiedener Fragebogen (RLS-DI, IRLS, RLS-6, SOMS, BSI, FSS, SF-12 und Schlaffragebogen) wie auch mittels Aktimetrie (PLMS) und Blutanalysen.

Ergebnisse: Die Resultate ergaben für die Gruppe «ohne psychische Störungen» signifikant mehr PLMS. Für die Gruppe «mit psychischen Störungen» zeigten sich stärkere Ausprägungen bezüglich Schweregrad des RLS, Müdigkeit, Beeinträchtigung der Lebensqualität und Somatisierungstendenzen. Es wurden keine signifikanten Gruppenunterschiede bezüglich klinischer Hauptkriterien, positiver Familienanamnese, Altersverlauf, Schlafstörungen und der Blutanalysen (inkl. Eisenstatus) gefunden.

Schlussfolgerung: Das Auftreten von periodischen Beinbewegungen ist ein potentieller Marker zur Unterscheidung von RLS und «RLS-like».

25 Reversible cerebral vasoconstriction syndrom as a cause for atypical subarachnoid hemorrhage – two case reports

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Introduction: Reversible cerebral vasoconstriction syndrome (RCVS) is a disorder characterised by sudden-onset and servere headache with or without additional neurologic symptoms and signs. Imaging techniques show multifocal and reversible vasoconstriction of cerebral arteries. The etiology is frequently idiopathic. RCVS can cause ischemic strokes, parenchymal hemorrhages and nonaneurysmal cortical subarachnoid hemorrhages (SAH).

Methods/Results: We describe two patients with idiopathic RCVS presenting with thunderclap-headaches and additional neurologic symptoms. In both cases magnetic resonance imaging (MRI) delineated a small cortical SAH. Transcranial duplex sonography (TCD) and digital subtraction angiography (DSA) revealed segmental stenoses of multiple cerebral arteries with complete resolution after a few weeks. There was no evidence for a different etiology of SAH or vasospasms such as intracranial aneurysms, other vascular malformations, cerebral venous thrombosis or drugs.

Conclusions: RCVS can cause SAH, which, in contrast to aneurysmal SAH, have a cortical localisation. Vasoconstriction is likely a cause and not a result of the hemorrhage, although the pathophysiology is not clearly understood.

26 Sepsis induces long-term verbal memory deficits and left-sided hippocampal volume reduction in quantitative voxel-based brain MRI

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Background: Until recently, critical care practitioners have focused on the survival of patients and not on long-term outcomes. However, current research indicates that critical illness can lead to permanent cognitive impairment. Cognitive impairment may be particularly common in survivors of sepsis. Long-term follow-up examination in rodents indicated that experimental induction of sepsis induces permanent behavioural deficits and neuroanatomical changes, such as reduced density of hippocampal neurons and reduced cortical cholinergic innervations.

Patients and methods: In this mono-center, retrospective study we recruited 51 patients between 18 and 75 years old for testing of cognitive functions and quantitative voxel-based brain MRI 9 to 18 months after treatment on an intensive care unit (ICU). During acute disease 25 patients were diagnosed with sepsis. The remaining 26 patients were treated for non-inflammatory diseases and served as control group. Cognitive testing was performed by NeuroCogFx, Trail making Test-A and B (TMT-A, TMT-B). Test results were compared with specific normative data and between groups. Magnetic resonance imaging measurements were performed using a 1.5-T scanner with sagittal T1-weighted image sequences yielding 200 slices and a voxel size of $0.9 \times 0.9 \times 0.9$ mm, followed by statistical parametric mapping.

Results: Both, sepsis and other ICU survivors show significant deficits in almost all cognitive domains. To test for sepsis-specific effects, we analysed the different patient groups separately (sepsis-survivors, survivors of severe sepsis, and non-septic ICU-survivors). Survivors of severe sepsis showed verbal memory deficits in comparison to non-septic ICU-survivors ($p = 0.01$), and in comparison to survivors of sepsis for trend (0.07). This was accompanied by a volume reduction of the left-sided hippocampal and parahippocampal areas ($p < 0.05$) in sepsis survivors in quantitative MRI brain volumetry.

Discussion: In this study we confirmed that ICU treatment leads to long-term cognitive impairment in various cognitive domains. More importantly, it shows that survivors of severe sepsis show an impairment of verbal memory associated with a reduction of left sided hippocampal volume. These findings argue for sepsis-specific effects of cognitive impairment after ICU treatment and demonstrate that survivors of severe sepsis are at particular risk for long-term cognitive impairment after full recovery.

27 Serum Copeptin levels correlate with disability in Multiple Sclerosis

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Background: The degree of activation of the hypothalomo-pituitary-axis (HPA) has been helpful in assessing disease severity and prognosis in several diseases but the measurement of circulating Corticotrophin-releasing hormone (CRH) and arginine-vasopressin (AVP) levels, the main secretagogues of the HPA-axis, is challenging. Copeptin is released in an equimolar ratio to AVP from the same precursor peptide and is more stable in the circulation and easier to determine. We investigated if copeptin levels correlate with disability in multiple sclerosis and if it predicts conversion to clinically definite multiple sclerosis (CDMS) in patients with a first demyelinating event (CIS).

Methods: We measured Copeptin levels in the serum of 28 patients with a CIS (EDSS 0–2.5: normal to minimal disability) and 15 MS patients with clinically confirmed diagnosis (CDMS) and EDSS scores of >/= 3.5 (at least moderate disability) using a highly sensitive sandwich immunoassay.

Results: Median Copeptin levels in MS patients were significantly higher compared to patients with a CIS (4.4 pmol/l (IQR 3.1–8.6 pmol/l) versus 3.3 pmol/l (IQR 2.4–4.2 pmol/l), $p = 0.035$). Time of conversion to CDMS was not mirrored by Copetin levels (Converters, n = 14: 3.2 pmol/l (2.6–3.8), No-Converters, n = 14: 3.2 pmol/l (2.3–4.4)).

Conclusion: The raised Copeptin levels observed in patients with established MS and disability may reflect, disease activity related release of inflammatory mediators, or a secondary response to disability, or both. Further studies comparing MS patients with different levels of disability progression must show if copeptin levels are a useful – maybe even prognostic marker for disability and disease severity in MS

28 Sleep disturbance impedes stroke recovery in the rat

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Introduction: Sleep disturbance (SDis) represents a risk factor for stroke recovery. We have previously showed that SDis over 3 days aggravates brain damage in the rat. The aim of this study is to further investigate the effects of SDis on the function recovery.

Methods: 17 male Sprague Dawley rats were subjected to ischemic surgery by occlusion of the distal branches of Middle Cerebral Artery (MCAo). 12 hours after ischemia, one group of

rats (n = 9) was subjected to SDis (12 h of sleep deprivation over 3 days) by gentle handling and another group (n = 8) left undisturbed after ischemia to serve as control. Single Pellet Reaching test (SPR) was used to assess motor function.

Results: After two-three weeks of training, the success of SPR reached about 50% (normalized as 100% for baseline). It dramatically dropped to 4% of baseline after MCAo in both groups. SPR continually recovered in the control group, reaching 50.36% ± 23.95 at the end of 4 weeks. In contrast, it remained at 24.70% ± 24.34 in the SDis group. Repeated measures ANOVA indicated a significant difference ($p = 0.001$) in group*time interaction ($F [6, 90] = 4.470$). Post hoc independent t-tests showed that group difference was significant at day 14 (Control 44.54 ± 16.52 vs SDis 19.36 ± 25.5, $p = 0.031$), 21 (Control 55.3 ± 25.57 vs SDis 21.05 ± 20.89, $p = 0.008$) and 28 (Control 50.36 ± 23.95 vs SDis 24.70 ± 24.34, $p = 0.045$), but not at days 1, 4 and 7.

Conclusion: Sleep disturbance over 3 days has a significant detrimental effect on long term recovery of motor function in the rat.

29 Sleepwalking in patients with Parkinson's disease

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Introduction: Sleepwalking (SW) corresponds to a complex sleep-associated behavior, characterized by locomotion, mental confusion, and amnesia. In a single center series of 165 consecutive patients with Parkinson's disease (PD), we found de novo SW in 6 subjects (4%, Arch Neurol 2008). In a questionnaire survey supported by the patient's organization Parkinson Switzerland, 36 (9%) out of 417 patients with SW were identified. The clinical and polysomnographic characteristics of PD patients with SW are essentially unknown.

Aim: To assess the polysomnographic characteristics of SW in PD patients.

Patients and methods: Out of 417 patients participating in the survey, 8 PD patients with SW (in four of them since childhood) and 6 PD patients without SW were assessed. A detailed clinical examination (including UPDRS III and mini mental state examination), standardized questionnaires (including validated sleep questionnaires, the Beck depression and anxiety inventory) and a conventional overnight polysomnography were performed.

Results: Compared to PD patients without SW, those with SW had a similar disease duration and motor symptom severity (UPDRS III), but higher scores on the Beck Depression Inventory ($p < 0.001$). Mini mental state examination scores did not differ between the two groups. Night-time hallucinations were reported in 7 out of 8 patients with SW, but only in 1 PD patient without SW.

There were no differences in polysomnographic sleep parameters (sleep latency, sleep efficiency, sleep stages percentages, and indices of nocturnal breathing and leg movements). However, REM sleep behavior disorder (RBD) was found in six PD patients with SW (in all 4 with de novo SW).

Conclusion: SW in PD appears to be associated with depression, night-time hallucinations and RBD. No differences were found, however, in polysomnographic parameters between PD patients with and without SW.

30 Soluble CD70: a novel immunotherapeutic agent for experimental glioblastoma

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Purpose of the study: Expression of CD70 on the surface of glioma cells was shown to induce a potent anti-tumor immune response in a murine glioma model in vivo. There is evidence that also the soluble form of CD70 is active in vivo. A soluble co-stimulatory ligand is attractive as it might have a wider distribution into the tissue surrounding the tumor in vivo.

Methods: The murine glioma cell line SMA-560 was engineered to produce a soluble from of CD70 (sCD70). The expression of sCD70 was confirmed by immunoblot. Markers of immune cells were assessed by flow cytometry. The proliferation of immune cells was investigated in a 3H-Thymidine assay. The secretion of IL-2 and IFN-gamma was assessed by ELISA. SMA-560 cells were implanted stereotactically in the right striatum of syngeneic VM/Dk mice. The infiltration of immune cells in gliomas was assessed by immunohistochemistry. CD8+ or NK cells were depleted by the injection of appropriate antibodies intraperitoneally.

Results: In vitro expression of sCD70 enhances proliferation of syngeneic splenocytes and their secretion of IL-2 and IFN-gamma. In syngeneic VM/Dk mice bearing intracranial gliomas, sCD70 enhances the survival rate. The infiltration of CD8+ cells is enhanced compared to controls. Depletion of CD8+ cells abrogates the survival advantage.

Conclusion: These data suggest that sCD70 is a potent stimulator of anti-glioma immune response with cytotoxic CD8+ T-cells playing a major role.

Postersession, Freitag, 6.11.2009, 13.00–14.00 Uhr

Gruppe 4

31 Suppression of gesture pantomiming by inhibitory theta-burst rTMS over left inferior frontal lobe

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Background: The traditional view of a predominant inferior parietal control of gesture production has been recently challenged by neuroimaging studies demonstrating that gesture pantomime may critically depend on inferior frontal function. The aim of the present work was therefore to investigate the effect of transient disruption by repetitive transcranial magnetic stimulation (rTMS) over these brain sites on pantomime and imitation of gestures.

Methods: In 10 right handed healthy subjects (5 women, aged 25–39) an inhibitory continuous theta-burst protocol of rTMS (cTBS) was applied over left inferior parietal lobule (IPL) and inferior frontal gyrus (IFG) versus baseline (BSL).We employed a repeated measures design with 1 week intervals between the 3 sessions in balanced order. Gesturing was assessed off-line within 15 minutes after cTBS using a recently developed test of upper limb apraxia (TULIA), which includes a pantomime and imitation subtests. Based on its highly sensitive scoring method the TULIA test shows no ceiling effect (cut off for apraxia <194, maximum score 240). Performance was assessed by a blinded rater based on video recordings.

Results: The findings revealed that cTBS significantly affected total TULIA scores ($F = 9.350$, $p = 0.02$, repeated measures ANOVA), which is mainly explained by the effect on the pantomime subtest ($F = 11.082$, $p = 0.009$), as imitation scores remained unchanged ($F = 1.887$, $p = 0.2$). Furthermore, significant differences were found between left IFG and IPL stimulation for total scores (225.6 ± 7.8 and 231.0 ± 6.4, $p = 0.02$, post hoc paired t-test) and particularly pantomime subscores (111.7 ± 4.8 and 115.0 ± 3.9, $p = 0.004$). When contrasted with BSL, a decrease of total scores at the level of a statistical trend was found for cTBS of IFG (225.6 ± 7.8 and 228.6 ± 5.5, $p = 0.09$) or a just significant increase for cTBS of IPL (231.0 ± 6.4 and 228.6 ± 5.5, $p = 0.05$).

Conclusion: The suppression of gesture pantomiming by cTBS over left IFG points to an inferior frontal rather than inferior parietal gesture representation. Furthermore, the findings suggests that inhibition of IPL favours the inferior frontal function during gesture pantomime indicating that such intrahemispherical facilitation may have clinical implications.

32 The NADPH oxidase Nox-1 is a mediator of brain injury in experimental stroke

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Cerebral ischemia and reperfusion is associated with the generation of reactive oxygen species (ROS). ROS are considered to contribute to the brain damage process. Mitochondria and the classic leukocyte-type NADPH oxidase are thought to be the significant sources of ROS in this scenario. Although the NADPH oxidase Nox-1 also produces ROS, little is known regarding its role for cerebral ROS formation and ischemia/reperfusion-induced brain injury. We studied this aspect in Nox-1 knockout-mice and their wildtype littermates.

After isolation of cells from the murine brain, we demonstrated the expression of Nox-1 in astrocytes, neurons as well as endothelial cells using RT-PCR. Transient focal cerebral ischemia was induced by the middle cerebral artery filament occlusion followed by reperfusion. Lesion volume was assessed using TTC staining. Furthermore, we examined the integrity of the blood-brain-barrier in vivo with sodium fluorescein (SF) and Evans blue (EB) as permeability markers.

Vascular architecture was similar between WT and KO animals as were filament-induced changes in cerebral blood flow in this model of transient focal cerebral ischemia. Lesion volume after one hour of ischemia and 23 hours of reperfusion however was significantly reduced in brains of KO as compared to those of WT mice (WT 77 mm^3 ± 10, KO 43 mm^3 ± 10 mean ± sem; $p < 0.05$). In line with this observation, the clinical brain injury score was significantly lower in KO than in WT mice (modified Bederson score, WT: 1.5, KO: 0.9; $p < 0.05$). Early BBB damage was significantly smaller in brains of KO as compared to those of WT littermates (SF: WT 149 ng ± 19, KO 72 ng ± 17; $p < 0.05$). Accordingly, brain edema formation was attenuated in KO mice (WT: 57 mm^3 ± 7, KO: 35 mm^3 ± 5; $p < 0.05$).

These data demonstrate that the Nox-1-containing NADPH oxidase is expressed in the murine brain and contributes to the pathophysiology of stroke. Inhibition of the NADPH oxidase may serve as a new approach to reduce brain injury after stroke.

33 The thermolabile variant of 5,10-methylenetetrahydrofolate reductase as possible risk factor for amyotrophic lateral sclerosis: a case-control study

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Introduction: Amyotrophic lateral sclerosis (ALS) is characterized by progressive neuronal degeneration. This study aimed at analyzing whether genetic variants of homocysteine metabolism are associated with the development of ALS.

Subjects and Methods: 162 patients diagnosed with ALS by modified Airlie House El Escorial criteria and 162 healthy subjects were enrolled. Genomic DNA from peripheral leucocytes was used for genotyping of seven genetic variants of Hcy metabolism by allele specific PCR with subsequent restriction analysis. In binominal regression analysis, the association between the genetic variants and ALS was analyzed with age and gender as covariables and threshold = 0.05.

Results: The frequency of the genotypes of the variant MTHFR c.677C>T (p.A222V) was different between patients and controls, i.e., the T-allele was more frequent in the patients than in controls: patients, CC/CT/TT: 0.40/0.48/0.13; controls, CC/CT/TT: 0.50/0.44/0.06 (Wald = 5.39; $p = 0.020$).

Discussion: In this study we found the thermolabile variant of MTHFR as possible risk factor for ALS. This polymorphism is known to lower MTHFR activity and to contribute to elevated plasma Hcy levels, which have been observed in ALS patients. These results suggest that the T-allele of MTHFR c.677C>T may contribute a risk of ALS, which should be tested in additional study samples.

34 Thrombolytic therapy in stroke patients older than 85 years

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Introduction: There is only few data about the outcome of very old patients being treated by thrombolysis after stroke.

Methods: We retrospectively analyzed the outcome of patients aged over 85 years, who underwent intravenous (IV) or intraarterial (IA) thrombolysis in our stroke center between February 2004 and November 2008.

Results: Of 34 included patients, 71% (n = 24) were aged 85 to 90 years and 29% (n = 10) were older than 90 years. 44% had an occlusion of the middle cerebral artery (M1 segment 21%, M2 segment 23%). 82% of the patients were treated by IV thrombolysis, 15% by IA thrombolysis. One patient underwent a combined IV and IA thrombolysis. Favourable outcome was defined as modified Ranking Scale (mRS) <=2 or mRS 3 for the subgroup of patients with historical prestroke mRS 3. Three months after stroke 29% of the patients reached a favourable outcome. 21% had a mRS of 4 or 5 and 26% died. In the subgroup of patients older than 90 years outcome was favourable in 40%.

Conclusion: As expected, mortality is higher and the outcome of patients aged over 85 years after thrombolysis is not as beneficial as in younger patients. Nonetheless, our data suggest that some very old patients might benefit from thrombolysis. Therefore very high age should not be an exclusion criteria for thrombolytic therapy after stroke.

35 Varicella zoster virus – hide and seek in an immunocompetent patient

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Introduction: Encephalitis and angiitis are possible, but uncommon complications of varicella-zoster-virus (VZV) infection, usually proceeded by a rash [1, 2]. Cerebro-spinal fluid (CSF)-PCR is an important diagnostic tool to confirm the diagnosis. We present a patient with a history suggestive of VZV-angiitis and -encephalitis without a rash and negative PCR.

Case report: The immunocompetent patient presented with a history of headache, temperature up to 38 °C, ataxia with falls and a progressive confusional state with reduced vigilance for three weeks. The CSF was abnormal with 42 cells (mononuclear) and a protein of 2 g/l. A broad search for pathogenic agents revealed positive values for VZV IgM in Serum, CSF-PCR was negative. On MRI, multiple small ischemias were present. On MR-angiography, conventional angiography and neurosonology multiple stenoses of the basal arteries were found.

A therapy with acyclovir was initiated, four days later the patient was orientated, awake, GCS 15. However, after discussion of the PCR and IgM-results concerning VZV, a non-specific polyclonal stimulation was assumed, and acyclovir was stopped. In the course of another three days the patient deteriorated again, this time also developing a slight hemiparesis on the left side. Acyclovir was initiated again. Over a period of 10 days the patient recovered, was alert, orientated, able to walk with slight ataxia, the hemiparesis wore off. Furthermore, the stenoses decreased. The neurosonologic examination before discharge was normal. Additionally, no further ischemic lesions occurred on MRI.

Discussion: Most likely this patient suffered from VZV-angiitis and encephalitis, despite the lack of a rash or a positive PCR-result. However, a rash has been described to occur in only about 60% of patients [2], and the sensitivity of VZV-PCR varies between 50 and 90% in the literature.

Conclusion: In a patient with typical clinical features of a VZV-angiitis and -enzephalitis, the lack of a rash or a negative PCR does not necessarily rule out the diagnosis.

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36 The increased number of regenerated axons after thyroid hormone treatment of transected sciatic nerve is accompanied by improvement of muscle reinnervation

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Injuries of peripheral nerves are common in clinical practice, and axonopathy is the usual mechanism explaining loss of motor function and muscle atrophy. Since reinnervation is essential for the return of nerve function, the main goal of peripheral nerve repair is to induce as many axons as possible to regenerate, enter the distal stump and proceed to reinnervate the end organs.

In our previous works, we have already shown that the administration of thyroid hormone (T3) in either silicon or biodegradable nerve guides significantly increased the number and the myelination of regenerated axons (J Neurotrauma. 2007;24:567–77). Therefore, it is important to investigate whether the increase in number of regenerated axons after T3-treatment of transected rat sciatic nerve is accompanied by an improvement in hind limb muscle reinnervation, as assessed by changes in morphology and number of neuromuscular junctions (NMJ).

NMJ were examined in PBS-control and in T3-treated rats on serial longitudinal hind limb muscles (gastrocnemius and plantar) stained with rhodamine-conjugated α-bungarotoxin and anti-neurofilament antibody: At 4 weeks of sciatic nerve regeneration, only rare regenerated axons were observed in PBS-control rats, and all end-plates were still denervated. In T3-treated rats, few reinnervated NMJ can be observed. Fourteen weeks following nerve regeneration, the histological analysis revealed the presence of a higher number of regenerated axons in T3-treated rats than in control rats. The morphometric measurement and the statistical analysis revealed a significant increase in the size and shape complexity of NMJ in T3-treated rats as compared to PBS-controls. Moreover, the density of acetylcholine receptors on postsynaptic membrane was significantly higher in T3-treated rats.

These results suggest that the T3-treatment stimulates not only the number of regenerated axons but also improves hind limb muscle reinnervation.

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37 Syndrome of the Trephined

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After a large craniectomy, a cranioplasty is not only cosmetic but also prevents or improves the syndrome of the trephined. This syndrome is a possible delayed complication of decompressive craniectomy. It consists of neurologic symptoms and deficits like controlateral weakness.

We report the case of a 37-year-old man who had suffered severe traumatic brain injury, needing a large craniectomy because of right hemispheric oedema. He presented with discrete left hemiparesis and neglect; his gait was safe. During the following weeks, left-sided weakness became more important with plegia of the hand and increasing difficulties to walk. A CT revealed no new lesion and EEG showed no epileptic activity.

Following cranioplasty, his condition improved markedly: within a few days, hemiplegia nearly fully recovered and neglect improved considerably.

Grant and Norcross (Ann Surg 110, 1939) first described the syndrome of the trephined. The physiopathology remains unclear: direct influence of the atmospheric pressure, altered CFS circulation, decreased cerebral perfusion, metabolic changes, have been proposed to explain the syndrome.

In our patient, the very large defect and prolonged upright body position have probably contributed to the occurrence of the syndrome.

38 Modafinil ameliorates posttraumatic sleepiness and fatigue: A double-blind, randomized, placebo-controlled pilot study

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Background: Excessive daytime sleepiness (EDS) and fatigue are frequent complaints following traumatic brain injury (TBI). In our prospective study on sleep-wake-disturbances 6 months after trauma, we found EDS in 38%, and fatigue in 17% of 65 consecutive TBI patients. Given the high frequency of TBI in the population and the enormous socioeconomic impact of vigilance impairment in TBI patients, treatment strategies are urgently warranted but do not exists until now. We aimed at studying the effect of daily modafinil on posttraumatic EDS and fatigue.

Methods: We ran a double-blind, randomized, placebo-controlled pilot study in 20 TBI patients with posttraumatic EDS or fatigue. Fatigue was diagnosed with the fatigue severity scale (FSS), and EDS with the Epworth sleepiness scale (ESS). The Beck Depression and Anxiety Inventory was used to assess depression and anxiety symptoms. At baseline and six weeks following treatment initiation (100–200 mg modafinil vs placebo), we applied these questionnaires and performed actigraphy, conventional nocturnal polysomnography, maintenance of wakefulness tests (MWT), and psychomotor vigilance tests.

Results: Demographic, psychiatric and sleep baseline characteristics did not differ between the two groups (each: n = 10). After 6 weeks of treatment, there was no significant effect on fatigue (as assessed by the FSS) in the modafinil group. However, the decrease in ESS scores was higher in the treatment group (–2.3 ± 2.3 vs 0.7 ± 1.8, p = 0.005). Objective estimation in the MWT confirmed the amelioration of EDS only in the treatment group. Psychomotor vigilance test results were similar in both groups.

Conclusion: Modafinil appears to be effective in the treatment of posttraumatic EDS and fatigue.

39 State space mapping of sleep and wakefulness in Parkinson patients and healthy controls

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Background: Sleep is commonly scored in stages, but the succession of behavioural states is only poorly understood. For a better description of sleep-wake dynamics, we have adapted state space analysis (SSA, originally applied in rodents) to analyze sleep in patients with Parkinson's disease (PD) and healthy controls.

Methods: We obtained polysomnographic recordings from 7 PD patients and 7 age-matched healthy controls. 30-s epochs were scored visually. EEG data were Fourier-transformed to obtain the power spectral density for each epoch. Thereafter, we calculated 3 ratios of frequency bands. While these ratios aim at capturing specific spectral features, their final nature is heuristic. After data processing via principal component analysis, smoothed time series were plotted as clusters and trajectories in a three-dimensional state space. The congruence between visual scoring and the classification based on EEG spectra was quantified with discriminant analysis (DA). We assessed ratios with best cluster discrimination (optimized for maximal surface of the triangle spanned between the centroids of the DA) and congruence.

Results: Power spectra revealed only small differences between PD patients and controls. Congruent scoring was obtained for a median of 90% of epochs in PD patients, and 93% in controls. The median surface of the triangle between centroids was 49 units for PD patients, and 180 units for controls. In all subjects, trajectory velocity within clusters was low for deep and REM sleep, indicating that EEG spectra of subsequent epochs in these sleep states show low variability. Highest velocities were found for wakefulness and epochs adjacent to state transitions.

Conclusion: SSA can be applied to sleep recordings of both healthy controls and PD patients. Embedding of further polysomnographic parameters such as submental muscle tone may improve discriminatory power. The further development of this method may improve our understanding of regulation of sleep and wakefulness in health and disease.

40 Population-based study of acute phase blood pressure after TIA and stroke in relation to pre-morbid measurements, underlying pathology and long-term outcome

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Background: Blood pressure (BP) is elevated in many patients with acute stroke, but the mechanism is uncertain. Moreover, the extent of "post-stroke" hypertension has not previously been related to detailed records of pre-morbid BP, and so it is uncertain how many patients have exhibited a tendency to similar or higher BPs in the past in the absence of stroke. In the first ever population-based study of pre- and post-stroke BPs, we compared acute post-stroke BPs with all recorded pre-stroke measurements.

Methods: We collected all acute phase post-event systolic (SBP) and diastolic (DBP) readings in all patients with an acute stroke or TIA in the Oxford Vascular Study and related these to clinical characteristics, stroke subtype and all recorded pre-stroke measurements by access to life-long general practice patient records. We also assessed the association between early post-stroke BP and risk of recurrent vascular events during long-term follow-up.

Results: 18,035 premorbid BP measurements were available from 1047 (98%) of 1069 consecutive eligible patients. First SBP in the acute phase was higher than the most recent pre-event reading in 65.4% (95% CI: 62.5–68.3) of patients but only exceeded the highest pre-event reading in 26.3% (95% CI: 23.6–29.0). This latter proportion varied with TOAST subtype of stroke ($p = 0.001$), ranging from 16.7% in cardioembolic stroke to 34.2% in lacunar stroke. In patients with a first post-event SBP measured within 3 hours of the ictus, mean (SD) acute SBP was higher in patients with TIA and minor stroke (NIHSS ≤3) than in those with major (NIHSS >3) ischaemic stroke (163.9 vs 156.5 mm Hg, $p = 0.017$), but was otherwise unrelated to stroke severity. First post-event BP was unrelated to risk of recurrent stroke or other vascular events.

Conclusions: Acute post-event SBP is lower than highest recorded pre-morbid SBP in the majority of patients, and is highest in patients with TIA and minor ischaemic stroke, suggesting that post-stroke hypertension is not a unique physiological response to major cerebral infarction.

41 Restless legs syndrome in pregnancy: A prospective, systematic study

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Introduction: Three retrospective studies suggested a high frequency (11–26%) of restless legs syndrome (RLS) in pregnancy. None of these studies used standardized methods for assessment of RLS and sleep. Characteristics and determinants of RLS during pregnancy are poorly known.

Methods: Women during (from the 1st trimester) and after pregnancy (8 weeks post-partum) are prospectively studied. Assessment includes 1) interview about RLS-symptoms and sleep habits/disturbances: 2) standardized questionnaires (incl. the international RLS-scale [IRLSS], Epworth sleepiness scale [ESS], and Pittsburgh Sleep Quality Questionnaire [PSQI]); 3) blood tests (incl. hemoglobin, estrogen, C-reactive protein and ferritin), 4) leg actigraphy (3rd trimester and post-partum).

Results: So far 498 women were screened. RLS was diagnosed in 52 women (10.4%), 38 were included in the study. 37% of them had a positive family history for RLS, 34% reported onset of RLS-symptoms before the 20th week, 18% suffered from RLS before pregnancy, 45% had RLS-symptoms daily, 42% had an IRLSS >20, and 100% had a PSQI >5 (all values in the 3rd trimester). Anemia (defined as Hb <11 g/dl in pregnant women) was found in 18% of affected and unaffected women. Ferritin levels <35 ug/l were found in 75% of RLS positive and in 94% of RLS negative women. Women with (pRLS) and without RLS (nRLS) had similar values in hemoglobin CRP, and ferritin (mean Hb 11.7 mg/dl in pRLS, 12 mg/dl in nRLS; Ferritin 22.6 µg/l in pRLS, 19.1 in nRLS). No significant difference of estrogen levels between pRLS and nRLS (measured in 15 pRLS and 10 nRLS in 3rd trimester. Leg actigraphy was performed in 7 cases pre and post partum, PLMI dropped dramatically.

Conclusion: Preliminary results of this ongoing study suggest that RLS in pregnancy: 1) is present in 10% of women; 2) frequently appears early in pregnancy; 3) is often severe/ frequent; 4) may not be related (only) to anemia/low ferritin levels or estrogen levels; 5) has a significant impact on sleep quality.

42 Experience of Moyamoya angiopathy in Zurich

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Introduction: Moyamoya angiopathy MMA (Moyamoya disease, Moyamoya syndrome and Moyamoya moid [unilateral pathology]) has been considered to be prevalent in Japan and Asian countries. Now we know its existence also in European countries. Since 1993 we have experienced 68 cases submitted to multiple microvascular extracranial – intracranial EC-IC bypass revascularization procedures. We present the management of patients with MMA and the postoperative results based on our experience.

Method: Definitive diagnosis according to diagnostic criteria can be done now with magnetic resonance angiography MRA along with clinical symptomatology. Digital subtraction angiography DSA is still important to know the delicate angiopathology and for the planning of surgical revascularization procedure. H215O PET is carried out for measurement of regional cerebral blood flow rCBF and hemodynamic reserves. Non-invasive Doppler-sonography is important for regular following-up to know the hemodynamic situation.

Multiple bypass procedures of direct vascularization have been performed as therapy of choice for augmentation of CBF.

Results: The series contains 45 children (0.1–17 yrs Av 6.8 yrs; f/m 1.36) and 23 adults(21–66 yrs Av 39 yrs; f/m 4.75). The patients are also from Germany (14), Holland (8), Austria (5), Denmark (3), Italy (3), Norway (1), Sweden (1), Qatar (1): besides Caucasian, middle east origin (4) and Asian origin (3). One thirds of patients have basic disease such as neurofibromatosis type 1, trisomy 21, hemoglobinopathy etc, so that these cases can be categorized as Moyamoya syndrome. Two adult patients presented with intracerebral hemorrhage. Almost all other patients presented with ischemia-infarction.

One adult patient died of perioperative ischemic edema. Among others, three other patients had perioperative ischemic complication but showed good recovery. Other patients profited from augmentation of CBF by multiple bypass surgery.

Conclusions: We present the state of the art of management of MMA including diagnosis, surgical treatment and the consequential results. In addition, long term follow-up results are presented along with distinctions in clinical pathophysiology of MMA between patients from Europe and Japan.