177. Tagung der Schweizerischen Neurologischen Gesellschaft
177e Réunion de la Société Suisse de Neurologie

gemeinsam mit SGVHN und SBG Club
conjointement avec SSNCO et SBG Club

Abstracts
Interlaken, 19.–21. Oktober 2006

Freie Mitteilungen

Session: Donnerstag, 19.10.2006, 17.00–17.45 Uhr

Wartenberg's migrant sensory neuritis: clinical and neurophysiological findings in 10 patients

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Wartenberg's migrant sensory neuritis (1932) is a rare condition and case reports are scarce. It consists in a pure sensory multiple mononeuropathy with a benign, although relapsing and remitting course. We reviewed the patients investigated in our ENMG laboratory between January 1992 and May 2006 and found 10 patients diagnosed and matching Wartenberg's description. In our series, the age of onset of first symptoms varied between 22 and 64 years. Patients mostly complained of pain and dysaesthesiae. In all cases the deficit concerned superficial cutaneous nerves and appeared in an asymmetric pattern in different cutaneous areas. The areas most frequently affected were distal: superficial radial and plantar medial nerves in 7 out of 10 patients, digital branches of median nerve in 6, calcanean nerve in 4. Clinical and laboratory investigations did not disclose any underlying systemic condition. Electrophysiological studies were performed in all patients. Sensory nerve conduction studies demonstrated reduced or absent sensory nerve potentials in the affected territories, but normal sensory nerve conduction velocities. Motor nerve conduction studies and electromyography were normal. These characteristics are suggestive of focal axonal nerve lesions but the reason why they affect only sensory nerve fibres remains puzzling. Our 10 patients are similar in all aspects to those reported in the literature. Pathophysiology of this multifocal sensory neuropathy remains unknown.

Effect of thalamic deep brain stimulation on the lower urinary tract function

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The mechanisms of cerebral regulation of lower urinary tract function are still poorly understood. In this study we investigated the effect of thalamic deep brain stimulation (DBS) for essential tremor (ET) on urodynamic parameters.

We prospectively evaluated 6 patients with ET 15 to 85 months after DBS lead implantation into the ventral intermediate nucleus of the thalamus. Urodynamic parameters were assessed and compared during thalamic DBS (ON-state) and 30 minutes after turning off the stimulator (OFF-state).

In the ON- compared to the OFF-state, we observed a significant decrease in bladder volume at first desire to void ($p = 0.043$) and at strong desire to void ($p = 0.043$) and in maximum cystometric capacity ($p = 0.028$). No significant differences between the ON- and OFF-state were found for all other parameters assessed including change in detrusor pressure during filling cystometry, bladder compliance, maximum detrusor pressure, detrusor pressure at maximum flow rate, maximum flow rate, voided volume, post void residual and pelvic floor electromyographic activity.

Our results demonstrated a significant effect of thalamic DBS on bladder storage but not on bladder emptying parameters. This suggests that the thalamus is involved in central control of lower urinary tract function during the storage phase.

Quantification of pyramidal tract affection in multiple system atrophy (MSA)

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MSA affects the extrapyramidal, cerebellar and autonomic nervous system. Pyramidal tract signs are frequently present but are currently not used for defining a diagnosis of MSA.

We demonstrate and quantify the affection of the pyramidal motor system in MSA patients.

Six patients with probable and three with possible MSA were examined clinically and with the triple stimulation technique (TST) of at least one affected limb. Two patients had a predominantly cerebellar form of MSA (MSAc), the others had MSA with predominant parkinsonian features (MSAp). Two patients with idiopathic Parkinson's disease, one with Lewy body dementia and one with progressive supranuclear palsy served as controls. The TST combines magnetic brain stimulation with supramaximal peripheral electrical nerve stimulation in a double collision paradigm that allows quantification of conduction deficits of the upper motor neurons.

An abnormal central conduction deficit was found in 8 patients. An unequivocally positive Babinski's sign was present only in one of them. In 4 patients two limbs were examined, and in 3 of them a conduction deficit was detected only in one limb. The central motor conduction time was normal in all but one patient. The 4 patients with parkinsonism other than MSA had normal TST assessments.

TST is a sensitive method to assess upper motor neuron deficits in MSA. This may be diagnostically helpful to distinguish MSA from other forms of parkinsonism without pyramidal tract involvement.

Post-ictal memory testing can predict the post-operative outcome of verbal memory after temporal lobe surgery for pharmacoresistant epilepsy

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Temporal lobe epilepsy (TLE) is the most common cause of lesional epilepsy in adults and is frequently pharmacoresistant. Surgery is superior to drug therapy but carries concerns about post-operative memory deficit, especially of verbal memory. Prognostic tests for postoperative outcome include the invasive intra-arterial amytal test, while functional MRI of memory is under evaluation. We were interested to know if transient postictal memory deficits could predict post-operative outcome.

We carried out interictal, postictal (30–60 minutes) and postoperative (3–6 months) verbal and visuospatial memory assessments on 35 patients with TLE (20 left, 15 right, mean age 32 years, mean age of onset 18 years, mean duration of disease 14.4 years). Fifteen words/figures were learned by rehearsing 5 times and recall was tested after 40 minutes. Acquisition performance was considered as the sum of the 5 trials.

Postoperatively, only verbal memory deficits were observed with no major changes in visuospatial memory. Postictally, there was a significant difference in acquisition between left and right TLE that was not present interictally. Moreover, postictal verbal acquisition memory was correlated with the postoperative results in the whole patient group ($p = 0.003$) and in the left TLE patients ($p = 0.04$).

Our study indicates that postictal memory assessment is superior to interictal tests in lateralising memory performance. Moreover, postictal assessment of verbal memory can predict the postoperative outcome.

Poster

Session: Freitag, 20.10.2006, 13.00–14.00 Uhr

P 01 Identification of the Nucleus Ventro-intermedius (VIM) in the healthy human thalamus using Diffusion Tensor Imaging (DTI) and functional Magnetic Resonance Imaging (fMRI)

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Objective: The central role of thalamic Nucleus Ventro-intermedius (VIM) within motor loops is well known. VIM is also a therapeutic target to treat tremor by functional neurosurgery like Deep Brain Stimulation (DBS). However, identification of the surgical target using current neuroimaging techniques is difficult. Our aim is to improve neuroradiological identification of VIM by combining functional with morphological MRI imaging.

Methods: We analysed the connectivity of VIM using Diffusion Tensor Imaging (DTI) and correlated these data with high-resolution 3 Tesla anatomic MR-imaging and with functional activation of VIM during a self-initiated motor fMRI-task in a block-paradigm and analysis of data in Brain Voyager. Additionally activation in corresponding areas in cerebellum and cortex were examined.

Results: DTI showed a connectivity of VIM to motor cortex and cerebellum. fMRI demonstrated a simultaneous activation of hand-notch-motor-cortex, VIM and cerebellar nuclei. Moreover, there was a good agreement between functional activation pattern, morphology of VIM and connectivity of VIM.

Conclusion: The matching of morphology (including connectivity) and functional activation pattern facilitates the identification of VIM within motor loops. As a next step functional imaging of VIM in patients with tremor has to be evaluated. This approach may open the possibility of functional planning of DBS in patients with movement disorders.

P 02 Spinal arteriovenous malformation as a differential diagnosis of inflammatory CNS disease

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We report the case of a 43-year-old man who was referred to our clinic with suspected inflammatory disease of the central nervous system (CNS). He had a 6-month history of slowly progressive spastic paraparesis of the lower limbs and urge incontinence with rapid worsening over the last three days.

Laboratory studies and CSF examination including screening tests for vasculitis, neurotropic viruses, neuroborreliosis and neurosyphilis showed no abnormalities. The magnetic resonance imaging (MRI) study of the brain was normal. MRI of the spine revealed an increased signal on T_2-weighted images within the thoracic cord, extending from approximately T-8 to T-11 with no contrast enhancement but pronounced flow voids from T-5 to T-12 localised dorsal of the spinal cord, corresponding most likely to dilated intradural vessels of the venous plexuses and suggesting a spinal arteriovenous malformation.

The patient underwent selective spinal arteriography, which revealed a dural arteriovenous fistula at T-6 with a high-pressure/low-flow angioma over several segments. Subsequent endovascular embolisation led to a complete obliteration of the fistula and stabilisation of the clinical condition.

P 03 Pain as the only symptom of cervical artery dissection

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Background: Headache and neck pain are frequent symptoms of spontaneous cervical artery dissection (sCAD). Patients presenting with pain as the only manifestation of sCAD, however, have not been systematically studied so far.

Patients and methods: Patients were drawn from an ongoing registry of consecutive cases diagnosed with sCAD. We analysed pain topography, dynamics, severity and quality, imaging findings and outcome.

Results: Overall, 20 of 245 sCAD patients (8%) presented with pain as the only symptom. Twelve had vertebral artery dissection, 3 internal carotid dissection and 5 multiple dissections. The median delay from symptom onset to diagnosis was 7 days (range 4 hours to 29 days). Six patients presented with headache, 2 with neck pain and 12 with both, headache and neck pain. Onset of headache was progressive in 6, acute in 8 and thunderclap-type in 4; neck pain was progressive in 7 and acute in 7. Headache was throbbing in 13 and constrictive in 5 patients; neck pain was throbbing in 4 and constrictive in 10. Eleven had unilateral and 9 bilateral pain. Pain was different from earlier episodes in all but one case. All patients were pain-free at 3 months.

Conclusion: Pain may be the only symptom in sCAD, even when multiple arteries are dissected. Pain topography, dynamics, quality and intensity were heterogeneous. Our data lend support to recommendations favouring imaging studies of the cervical arteries in patients with new-onset unexplained headache or neck pain.

P 04 Expression of glutamatergic markers in the motor cortex of parkinsonian rats

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The classical Parkinson's disease (PD) model predicts that dopaminergic denervation in the basal ganglia modifies thalamic projections to the motor cortex. However, the exact physiological changes occurring in the motor cortex remain unclear.

In a previous study (Capper-Loup et al., Exp Neurol 2005) we have described an increase in the expression of parvalbumin (PV) in the primary motor cortex of parkinsonian rats as a marker of increased GABAergic activity. The aim of the present study was to analyse the changes induced by PD in the glutamatergic system of the motor cortex.

We used the 6-hydroxydopamine (6-OHDA) rat model of PD. To analyse the glutamatergic gene expression in the motor cortex, we performed in situ hybridisation histochemistry with DNA oligoprobes. We chose a pre-synaptic glutamatergic marker, the vesicular glutamate transporter (vGluT1) and a post-synaptic one, the N-methyl-D-Aspartate (NMDA) receptor subunit 1 (NR1).

Results showed that vGluT1 and NR1 gene expression was decreased on the lesioned side of the anterior part of the motor cortex. In contrast, vGluT1 and NR1 gene expression was higher on the lesioned side of the posterior part of the motor cortex compared to the unlesioned side.

Our data demonstrate that glutamatergic gene expression is modulated in the motor cortex of parkinsonian rats. These changes seem more complex than those predicted by the classical PD model.

P 05 The potential usefulness of ephedrine in a stepwise clinical improvement of a non-paraneoplastic Lambert-Eaton myasthenic syndrome (LEMS)

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Introduction: Ephedrine, a controversial drug, has been rarely tested in myasthenia gravis but never in the Lambert-Eaton myasthenic syndrome (LEMS).

Patient description: The case of a 60-year-old woman suffering from a LEMS with anti-VGCC antibodies and no malignancy is reported. A treatment of ephedrine showed an evident clinical improvement.

Methods: We evaluated the patient by a series of repetitive functional (Hammersmith motor ability score, HMS) and electrodiagnostic (Edx) analyses. The CMAP were recorded in an every day session, in different treatment conditions: no treatment ("OFF"); after 90 minutes: 60 mg of Mestinon® ("MES"), 25 mg of 4-DAP ("DAP") and 100 mg of Ephedrine ("EPH"); and 90 minutes after the associated treatment: 4-DAP and Mestinon®; Ephedrine with DAP ("EPH+DAP").

Results: A progressive improvement of the clinical score is observed: the worst result (20/40) obtained during the OFF-period and the best result (40/40) in the "EPH-DAP" state. The same range of improvement is proven during the Edx sessions; the mean CMAP amplitudes obtained at rest and just after contraction were the lowest during the OFF-state and maximal during the "EPH-DAP" condition.

Discussion and conclusion: Our study demonstrates a stepwise clinical improvement in the treatment of LEMS due to the sequential use of different drugs, with Edx parameters correlation. Furthermore, our study underscores the potential usefulness of ephedrine as a treatment option in LEMS.

P 06 Gender differences in ictal rCBF SPECT patterns of medial temporal lobe seizures

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The study describes brain areas involved in temporal lobe (mTL) seizures of 12 patients which show effects of gender. Image analysis employed principal component analysis (PCA) of ictal SPECT data to assess functional connectivity. PCA decomposed the covariance matrix containing images of patients and healthy subjects into distinct component images of independent variance. Two principal components (PCs), i.e. the first (7.7% of variance) and the third PC (6.5% of variance), discriminated the subject groups: patients with right or left mTL seizures and normal volunteers, indicating distinct neuronal networks implicated by the seizure. Moreover, the fourth PC (5.9% of variance) showed a difference between genders ($p < 0.05$). PC4 exhibited differences in temporo-limbic and frontal brain volumes in women, characterised by positive loading of the hippocampus, contralateral to the seizure origin, the orbito-frontal, the fronto-polar and the insular cortex. In males, the pattern expressed preferentially included the basal temporal lobe at the site of seizure origin, the primary and associative visual cortices, the posterior cingulate and the paracingulate cortex. The differential expression of distinct neuronal networks during seizure manifestation indicates a functional sexual dimorphism, which may correlate with specific neurobehaviour, for example in emotion processing. Its study is a compelling future activity.

P 07 Delayed recanalisation of middle cerebral artery occlusion after intra-arterial thrombolysis: has it any implications on the clinical outcome?

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Background: Early recanalisation is a significant predictor of favourable outcome in ischaemic stroke. Whether delayed recanalisation is also related to the outcome is unclear.

Objectives: To assess the prevalence of delayed recanalisation after intra-arterial thrombolysis (IAT) in patients with middle cerebral artery (MCA) occlusions and to compare the outcome of patients with delayed recanalisation to that of patients with persistent occlusion.

Methods: 280 consecutive patients were treated with IAT. 193 patients (69%) had an occlusion of the M1 or M2 segment of MCA. 52% underwent a TCD examination within 10 days. Early recanalisation was assessed angiographically using the TIMI criteria. Thrombolysis in Brain Ischaemia (TIBI) grading system (based on TCD) was used to assess the delayed recanalisation. Clinical outcome was measured by the modified Rankin Scale at 3 months.

Results: 58 patients (65%) had a good early recanalisation (TIMI 2/3). 22/31 patients with poor early recanalisation (TIMI 0/1) achieved good delayed recanalisation (TIBI 2/3). On the other hand, 9/58 patients with TIMI 2 or 3 regressed to TIBI 0 or 1. Overall, 71 patients (80%) achieved a good delayed recanalisation. The outcome of patients with delayed recanalisation did not differ from that of patients with persistent occlusion.

Conclusion: Delayed recanalisation occurs in a significant proportion of patients with M1/M2 occlusion, but it does not seem to be associated with additional clinical benefit.

P 08 Multiple disease categories screening analysis (Multiscan) by tandem mass spectrometry in urine, plasma and dried blood spots

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Introduction: Clinical symptoms of many inborn errors of metabolism (IEOM) are partially unspecific like intractable grand mal epilepsy, absence seizures, ataxia, muscular hypotonia, mental retardation and progressive extrapyramidal movement disorders. We developed multiple disease categories screening analysis (MULTISCAN) – an advanced selective screening method using Tandem Mass Spectrometry (TMS) in urine and plasma – for detecting IEOM.

Method: Urine metabolites were separated by a column and quantified by TMS. We show new applications with TMS screening for common and rare metabolic diseases. Plasma metabolites like homocysteine, phytanic acid and very long-chain-fatty acids (VLCFA) in plasma are screened in a few minutes.

Results: In just a few minutes all relevant pathognomic metabolites are detected. Key metabolites in urine, e.g. pipecolic acid for a preselection in peroxisomal disorders, guanidinoacetate and creatine for the diagnosis of guanidinoacetate methyltransferase deficiency (GAMT) as well as purines and pyrimidines are detected, too. Globotriaosylceramides (GL-3) in urine and plasma for diagnosis and therapy monitoring in Fabry disease are screened by a comparable method. Peroxisomal disorders may be confirmed by quantification of phytanic acid and VLCFA in plasma.

Conclusion: Tandem mass spectrometry in urine, plasma and dried blood spots is a rapid, sensitive, high throughput and reliable diagnostic tool in psychomotoric retarded patients.

P 09 An anti-Hu syndrome preceding a carcinoma of the vocal cords

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The anti-Hu syndrome is a paraneoplastic neurological syndrome, most frequently associated with small cell carcinoma of the lung. Paraneoplastic syndromes are extremely rare in otolaryngology.

We report the case of a 63-year-old man who presented with asymmetrical paraesthesias of the hands later spreading to the arms in 2002. Neurophysiological studies showed a mixed axonal/demyelinating sensory-motor

neuropathy. No underlying condition was found but a paraneoplastic screen showed anti-Hu antibodies. 6 months later he noticed a hoarseness, bronchoscopy showed no pathology. In 2005 finally a squamous cell carcinoma of the vocal cords was diagnosed. Retrospectively an association of this cancer with the anti-Hu syndrome must be presumed. In various follow-ups the neuropathy remained stable. This case report shows that paraneoplastic neurological symptoms often appear before the associated cancer has been identified.

P 10 Long-term effect of intra-arterial thrombolysis in stroke

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Background: Thrombolysis has been shown to improve the 3-month-outcome of patients with ischaemic stroke, but knowledge of the long-term effect of thrombolysis is limited.

Methods: The present study compares the long-term outcome of stroke patients who were treated with intra-arterial thrombolysis (IAT) using urokinase with the outcome of patients treated with aspirin. The modified Rankin scale (mRS) was used to assess the outcome. 173 patients treated with IAT and 261 patients treated with aspirin from the Bernese Stroke Data Bank were eligible for the study. A matching algorithm taking into account patients' age and initial stroke severity (as measured by the National Institute of Health Stroke Scale, NIHSS) was used to assemble an IAT and an aspirin group. Matching was blinded for clinical outcome.

Results: 144 patients treated with IAT (mean age 63 years, 51% women) and 147 patients treated with aspirin (mean age 62 years, 37% women) could be matched and included in the comparative analysis. The median NIHSS score was 14 in each group. At 2 years, 56% of the patients treated with IAT and 42% of the patients treated with aspirin achieved functional independence (mRS 0 to 2; $p = 0.037$). Clinical outcome was excellent (mRS 0 to 1) in 40% of the IAT and in 24% of the aspirin patients ($p = 0.008$). Mortality was 23% and 24%, respectively.

Conclusion: The present study provides evidence for a sustained effect of IAT when assessed 2 years after the stroke.

P 11 Muscle functional magnetic resonance spectroscopy (fMRS) in myopathy

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Muscle metabolites may be an additional aid in clinical muscle and nerve diagnostics. Functional magnetic resonance spectroscopy (fMRS) allows non-invasive monitoring of the intracellular metabolic energy turnover during electrically imposed muscle activity. The aim was to compare measurements of patients with myopathy against normal values.

Methods: Proton spectra of the anterior tibial muscle were acquired with a standard clinical MR scanner at 1.5 Tesla with a 12 s temporal resolution before, during and after an isometric maximal tetanic muscle contraction imposed by electrical stimulation of the peroneal nerve with a supramaximal (30–60 mA) pulse train of 20 Hz during 2 min. Serum creatine kinase (CK) and myoglobin levels were measured before and after stimulation.

Results: The measurements were technically successful in a clinical setting. In healthy volunteers a robust response pattern was observed, with a decrease of the phosphocreatine(CrP)-associated peaks during and an incomplete recovery in the first minutes after stimulation, along with an increase in acetyl carnitine (AcCt), reflecting early involvement of oxidative fatty acid metabolism. In myopathy these metabolic responses were greatly reduced.

Conclusion: fMRS is a promising method for the assessment of muscle diseases. It may contribute additional valuable information, especially in metabolic myopathies.

Supported by the Swiss National Science Foundation (SNF grant 3200B0-107499/1).

P 12 Spinal cord infarction after skiing – or fibrocartilaginous embolism (FCE)

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Fibrocartilaginous embolism (FCE) is an uncommon cause of spinal cord infarction. We present the case of a 38-year-old previously healthy woman who reported acute severe back pain after skiing and developed a Brown-Séquard syndrome in the following 24 hours. Her clinical findings and neuroimaging studies were consistent with a spinal cord infarction in the territory of the anterior spinal artery. The main clinical features include sudden severe pain, a free interval of neurological symptoms and progression in time indicating a "spinal stroke in evolution", which often leads to severe para- or tetraparesis with urinary and bowel incontinence. In approximately one half of the cases possible precipitating factors like minor traumas have been postulated. The most likely hypothesis is that nucleus pulposus material may be exposed to the vertebral body vasculature by forceful herniation into the vertebral body and then enters the arterial system by arteriovenous communications during simultaneous excessive Valsalva, causing arterial embolisation of the spinal cord. The occurrence of a sudden painful myelopathy following minor trauma and/or Valsalva manoeuvre has to include FCE in the differential diagnosis when other common causes of myelopathy are excluded.

P 13 Voxel-based statistical evaluation of Benzodiazepine receptor (BDR) and interictal rCBF SPET in the presurgical evaluation of patients with pharmacoresistant temporal lobe epilepsy (TLE)

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Aim: BDR SPET provides functional information about the epileptogenic focus in patients with TLE, especially when ictal rCBF SPET is not feasible. This study aims to evaluate statistical parametric mapping (SPM) analysis of BDR SPET in patients with TLE.

Methods: We enrolled 10 patients (7 men, 3 women, 13–60 years old). In addition to the standard presurgical work-up, all patients underwent interictal rCBF and BDR SPET. These studies were compared to a normative dataset acquired in healthy volunteers using SPM99, comprising group and individual analyses. MRI findings, histological analyses of biopsy specimens, obtained during surgery and surgical outcome showed evidence for a right medial temporal lobe (RMTL) seizure origin in all patients.

Results: Engel class I outcome was observed for all patients over a 6- to 36-month follow-up after surgery. Statistical analyses of rCBF and BDR SPET data resulted in a focus localisation within the right medial temporal lobe in all patients. Group analyses showed a statistically significant decrease of BDR density in the RMTL, whereas interictal rCBF was reduced in the entire temporal lobe and bilaterally in the parietal/occipital cortex ($p < 0.05$). In the individual analyses, BDR SPET showed less variance than rCBF SPET ($p < 0.05$), indicating that BDR SPET is more reliable with regard to focus localisation.

Conclusion: Compared to interictal rCBF SPET, statistical evaluation of BDR SPET provides more precise localisation of the epileptogenic focus in TLE.

P 14 Successful intravenous immunoglobulin therapy in a patient with Anti-Hu-associated painful neuropathy without the evidence of underlying neoplasia

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We report the case of a 59-year-old woman who developed progressive clinical signs of a painful symmetrical sensorimotor peripheral neuropathy besides weight loss of 16 kg within four months, fever attacks and sweat-

ing during the night. The Anti-Hu antibody titre was elevated.

Concentric needle electromyography (EMG) revealed a mixed axonal/demyelinating sensorimotor neuropathy. Despite extensive work-up no evidence of neoplasia (especially small-cell lung cancer) was obtained in serology, CSF, X-ray (CT thoraco-abdominopelvin), mammography, cerebral and spinal MRI, FDG-PET, rectal and bone marrow biopsy. No evidence of vasculitis was found in serology, MRI of the brain or sural nerve biopsy.

Symptomatic analgesic treatment with pregabalin and corticosteroids had no significant effect. After intravenous immunoglobulin application (0.4 mg/kg) over a period of five days a major improvement of painful paraesthesia and hypaesthesia was observed.

P 15 Comparaison de l'effet du modafinil dans la sclérose en plaques et les accidents vasculaires cérébraux

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Introduction: La fatigue d'origine neurologique est fréquente et handicapante. Ses différents profils doivent encore être déterminés. Le bénéfice d'un traitement médicamenteux reste difficile à démontrer.

Objectifs: (1.) Analyse de la réponse de la fatigue neurologique primaire à une thérapie adrénergique (modafinil). (2.) Comparaison de son efficacité sur la fatigue subjective de deux populations: patients avec SEP de forme poussée-rémission (EDSS <4, Rankin ≤2), patients avec AVC (NIHSS <4, Rankin ≤2).

Méthode: 19 patients AVC (âge 51,2 ± 12,3; NIHSS 1 ± 0,94),18 patients SEP (âge 43,3 ± 10,1; EDSS 2,31 ± 0,71). L'échelle d'évaluation de la fatigue (FAI) est administrée au temps 0, à 3 mois de traitement et à un mois de l'arrêt du traitement. Trois des 4 facteurs de la FAI sont analysés (sévérité, spécificité, impact psychique). Les fonctions cognitives, l'humeur (HAD) et la somnolence (Epworth scale) sont corrélées aux scores FAI (t-test).

Résultats: Le modafinil améliore le score de sévérité du FAI (p = 0,0007); les modifications des scores du groupe SEP en sont déterminantes. Les patients avec AVC du tronc cérébral et du thalamus améliorent leur score de sévérité. Les autres facteurs analysés ne se modifient pas significativement.

Conclusion: Le modafinil peut avoir un effet bénéfique sur la fatigue mentale d'origine cérébrale, notamment chez les SEP. Son efficacité chez les AVC dépendrait du site lésionnel, particulièrement de structures cérébrales nécessaires à l'activation cérébrale.

P 16 Restless legs and restless legs-like syndrome

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Background and aim: Four essential diagnostic criteria are mandatory for the diagnosis of restless legs syndrome (RLS). In situations with diagnostic uncertainty, supportive clinical features (affected family members, response to dopaminergic therapy, periodic limb movements) may corroborate the diagnosis. We hypothesised whether the adherence to the essential criteria may lead to an overdiagnosis of RLS.

Methods: We retrospectively analysed 117 patients who fulfilled all the essential criteria for RLS. Validated self-rating scores of RLS symptoms (IRLSS) were obtained. Psychiatric evaluations were performed in all patients, in whom a psychiatric disorder was suspected. Polysomnographic evaluation of periodic leg movements index (PLMI) was performed. We differentiated patients with "classical RLS" (RLS-C; at least 2 supportive criteria) from those with "restless legs-like syndrome" (RLS-L; no supportive criteria).

Results: 103 (88%) patients had RLS-C and 14 (12%) had RLS-L. RLS-L patients were younger, duration of RLS symptoms was shorter and IRLSS was higher compared to RLS-C patients. Psychiatric abnormalities were more commonly found in RLS-L.

Conclusion: Our findings suggest that strict implementation of the essential criteria may lead to an overdiagnosis of RLS and suggest an important role of the supportive criteria. Further studies are needed to understand whether the RLS-L is a variant of RLS-C or – as we believe – a distinct disorder mimicking RLS-C.

P 17 Allograft inflammatory factor 1 in CIDP and vasculitic neuropathy

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The allograft inflammatory factor-1 (AIF-1) is a modulator of the immune response during macrophage activation. Previous gene expression studies have shown an upregulation of AIF-1 in sural nerve biopsies of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) and vasculitic neuropathy (VAS) compared to normal nerve (NN).

We performed immunohistochemistry on paraffin sections of human nerve biopsies of 10 vasculitis, 6 CIDP, 6 non-inflammatory axonal neuropathy (NIAN) and 3 normal nerves. An immunofluorescence colocalisation study was performed to investigate colocalisation of AIF-1 and activated macrophages stained for CD68.

There is a small constitutive expression of AIF-1 in normal human nerve. In CIDP and vasculitis nerve, however, AIF-1 expression was much higher when compared to normal nerve and non-inflammatory axonal neuropathy ($p < 0.05$). AIF-1 positive cells were increased in the endoneurium, perineurium, epineurium as well as in blood vessel walls. Most AIF-1 expression was seen in the endoneurium of inflammatory nerves. AIF-1 was also significantly increased in the blood vessel walls of vasculitis compared to CIDP cases ($p < 0.05$). By colocalisation studies we demonstrate that most of the AIF-1 positive cells were CD68 positive macrophages. Moreover, AIF-1 colocalised with vascular smooth muscle cells indicating a role in vasculits.

The higher expression of AIF-1 in CIDP and VAS compared to non-inflammatory axonal neuropathies and normal nerve confirms our gene expression study on the cellular level. In summary, AIF-1 seems to be associated with inflammatory polyneuropathies.

Comment: A part of the results of this study has been presented at the ENS 2006 in Lausanne.

P 18 Characterisation of the muscle involvement in dynamin 2-related centronuclear myopathy

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Centronuclear myopathy (CNM) is a slowly progressive congenital myopathy characterised by abnormal centrally located nuclei in a large number of muscle fibres. Recently, different missense mutations affecting the middle domain of the dynamin 2 (DNM2) have been shown to cause autosomal dominant CNM. In order to better define the phenotype of DNM2-related CNM, we report here on the clinical and muscle imaging findings of 10 patients harbouring DNM2 mutations. DNM2-CNM is characterised by slowly progressive muscular weakness usually beginning in adolescence or early adulthood. In addition to bilateral ptosis, our data show that distal muscle weakness often exceeds proximal involvement. Furthermore, electrophysiological investigations frequently demonstrated signs of mild axonal peripheral

nerve involvement, and electromyographical examination may show neuropathic changes in addition to the predominant myopathic changes. These features overlap with findings seen in the phenotype of DNM2-related autosomal dominant Charcot-Marie-Tooth disease type 2B. In all 10 DNM2-CNM patients muscle computer tomography assessment showed a consistent pattern of muscular involvement and a characteristic temporal course with early and predominant distal muscle involvement, and later affection of the posterior thigh compartment and gluteus minimus muscles. The recognition of this specific imaging pattern of muscle involvement – distinct to the reported patterns in other congenital myopathies – may enable a better selection for direct genetic testing.

Freie Mitteilungen

Session: Freitag, 20.10.2006, 17.00–18.00 Uhr

Gender differences in spontaneous cervical artery dissection

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Background: Spontaneous cervical artery dissection (sCAD) is a frequent cause of ischaemic stroke in both sexes, mainly affecting young and middle-aged subjects. Gender differences have not been analysed systematically yet.

Methods: Demographic data, risk factors and clinical presentation of 698 consecutive sCAD patients were recorded. Clinical outcome of ischaemic stroke patients (n = 408) was analysed at 3 months using the modified Rankin scale (mRS). Data were compared between the two sexes.

Results: Of a total of 696 patients, 399 (57%) were men and 297 (43%) women ($p < 0.0001$). Women were younger than men (42.5 ± 9.9 years versus 47.5 ± 9.3 years; $p < 0.0001$). Men showed a higher frequency of hypertension (31% versus 15%; $p < 0.0001$), and migraine was more frequent in women (47% versus 20%; $p < 0.0001$). Presenting symptoms and signs were similar in both sexes except for a higher frequency of pulsatile tinnitus in women (16% versus 8%; $p = 0.001$). Multiple dissections occurred more often in women than in men (18% versus 10%; $p = 0.001$). The percentage of stroke patients with a favourable outcome at 3 months (mRS 0 or 1) did not differ between women (58%) and men (54%; $p = 0.51$).

Conclusions: Women with sCAD are younger than men and have more often multiple dissections. The usual female preponderance of migraine and a male preponderance of hypertension were observed. There were no major differences based on gender in presenting symptoms and signs or functional clinical outcome.

Slower disease progression and prolonged survival in contemporary ALS patients: is the natural history of ALS changing?

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Objectives: To analyse whether disease outcome in ALS has changed over the last 20 years.

Methods: We compared disease progression and survival in 1041 patients diagnosed with ALS between 1984 and 1999 (historical group, n = 647) and between 1999 and 2004 (contemporary group, n = 394).

Results: The median survival time from symptom onset was 4.32 years in the contemporary group, compared to 3.22 years in the historical group ($p < 0.001$). The contemporary patients progressed slower (10 months to 20-pt. increase in AALSS) compared to patients in the historical group (9 months, $p < 0.001$). The observed outcome improvement over time was independent of confounding factors, such as age, sex, diagnostic delay, site of symptom onset, baseline FVC, baseline AALSS, and independent of the use of potentially outcome-modifying therapies: riluzole, NIV, PEG.

Conclusion: Contemporary patients had significantly prolonged survival and slower disease progression compared to patients from the historical group. Despite some limitations, the improved outcome in contemporary patients seems to be independent of the use of potentially outcome-modifying therapies. This observation suggests the possibility that disease progression has changed over time and that the disease has become less aggressive. Further studies are needed to determine whether there has been a fundamental change in the natural history of the disease or whether our results are due to other, unmeasured aspects of improved multidisciplinary care.

Correcting incapacitating orthostatic hypotension with ambulatory noradrenaline pump in pure autonomic failure. Case report

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A 46-year-old man with no past medical history developed progressive orthostatic hypotension (OH) due to PAF (Bradybury-Eggleston syndrome). Multiple system atrophy and peripheral neuropathies were excluded based on a 7-year follow-up and extensive investigations. Maximal medical treatment, tight elastic trousers, resulted in supine hypertension and did not prevent disabling orthostatic syncopies starting at age 52.

On a tilt-table in upright position, convulsive syncopy, unmeasurably low blood pressure (BP), severely deficient heart rate (HR) adaptation, absent norepinephrine response and excessive ADH-response were documented. MIBG scintigraphy showed complete cardiac sympathetic denervation. After exclusion of systemic arterial disease and determination of norepinephrine requirements, a subclavian port-a-cath was implanted and connected to a small portable medication pump.

With the pump running, tilt-table testing resulted in the absence of BP drop and of syncopy, in mild elevation of HR and in near-normalised ADH-values. All other medications could be discontinued and supine hypertension disappeared. No more syncopies occurred, the patient regained complete independence. Transient mild chest tightness without ECG-changes was noted at the beginning of each activation of the pump.

Near-physiological conditions and functional independence were re-established in a patient with disabling OH thanks to an ambulatory norepinephrine pump.

Pressor effect of water, but not of bouillon in multiple system atrophy

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Objective: Water drinking transiently increases blood pressure (BP) in patients with chronic autonomic failure due to multiple system atrophy (MSA), thereby improving orthostatic tolerance by mechanisms that still remain unclear. We compared this pressor effect of water with bouillon, a common "household remedy" to increase BP.

Methods: 6 MSA patients with severe orthostatic hypotension in a baseline tilt table testing underwent repeated tilt table testing 30 minutes after ingestion of 450 ml water and 30 minutes after drinking 450 ml fat-free vegetable bouillon respectively. Beat-to-beat cardiovascular indices were measured using the Finometer device.

Results: 30 minutes after water ingestion, all patients had subjectively and objectively improved orthostatic tolerance compared to baseline. In contrast, drinking of bouillon instead of water did not change the degree of orthostatic hypotension compared to baseline.

Conclusion: The pressor effect of water was confirmed in all patients. However, the same amount of bouillon did not have any beneficial effect on orthostatic tolerance within 30 minutes. The lack of a pressor response to bouillon within 30 minutes after intake may be due to superimposed postprandial hypotension in patients with severe autonomic failure. Advice of drinking bouillon may be helpful in many, but not all patients with orthostatic intolerance.

Central periodic breathing after stroke – brain damage and stroke topography versus cardiac dysfunction

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Background: Central sleep apnoea and central periodic breathing in sleep (CPBS) are present in up to 40% of patients with acute ischaemic stroke and often spontaneously recover during the following weeks. The aim of our study is to characterise CPBS and its clinical and prognostic implications in acute ischaemic stroke, and to better define the potential role of central nervous system in the complex respiratory changes accompanying brain ischaemia.

Methods: We included 77 consecutive patients admitted within 96 hours after stroke onset. Stroke severity on admission (NIH Stroke Scale, NIHSS) and stroke outcome at discharge (modified Rankin Disability Scale) were assessed. An ECG was performed on admission, a transoesophageal echocardiography during hospitalisation. Nocturnal breathing was assessed with an ambulatory device the first night after admission. Sleep apnoea was defined by an apnoea-hypopnoea-index *10/h, a differentiation between obstructive and central apnoeas was undertaken according to standard criteria. CPBS was defined as *3 cycles of regular crescendo-decrescendo breathing associated with reduction of *50% in nasal airflow and respiratory effort lasting *10 seconds. CPBS severity was represented as absolute time and percentage of recording time.

Results: 30 (39%) patients showed CPBS during *10%, 7 (9%) during *50% of recording time. Severity of CPBS correlated with severity of central apnoeas ($p > 0.0001$) and oxygen desaturations ($p > 0.0001$), but not with severity of obstructive apnoeas. CPBS severity was associated with age ($p = 0.026$), stroke severity (NIHSS, $p = 0.005$), ECG abnormalities ($p = 0.001$) and lower left ventricular ejection fraction ($p < 0.0001$). CPBS severity was higher in patients with extensive hemispheric strokes ($n = 6$, $p = 0.016$), and lower in patients with strokes involving the left insular ($n = 8$, $p < 0.0001$) and mesencephalic region ($n = 5$, $p = 0.003$).

Conclusions: CPBS is a frequent phenomenon in acute ischaemic stroke and is associated with older age, sleep apnoea severity, stroke severity and extension on admission, and occult cardiac dysfunction. The lower occurrence of CPBS in strokes with involvement of the left insular and mesencephalic region suggests a pivotal role of these brain areas in the modulation of respiratory response to acute ischaemic brain damage and emphasises the role of the central nervous system in the pathogenesis of central respiratory phenomena after stroke.

Neurologist-in-training

Answers to MCQ

1 E **2** D **3** A **4** D **5** C

Answers to Neuroradiology/Neuroanatomy

A Internal cerebral vein
B Left middle cerebral artery
C Superior colliculus
D Tentorium
P Craniopharyngioma

The patient's loss of consciousness was hard to classify. The absence of cloni made a seizure unlikely, although an atonic generalised seizure with a subsequent left Todd's paralysis is still possible. A migraine with a brain-stem aura in this patient with a history of migraines is not very likely, given the absence of other brain-stem signs, previous auras and headaches after the event. TIAs in the ponto-diencephalic region ("top of the basilar syndrome") can present with loss of consciousness and focal findings upon awakening. Usually, there are some focal symptoms before the loss of consciousness, and they should include oculomotor and papillary abnormalities.

The most likely syndromic diagnosis in this patient was a syncope due to hyperventilation, with a transient hemisyndrome upon awakening revealing a chronic lesion on the right corticospinal and sensory pathways.

The CT showed a tumour in the suprasellar region with an annular hyperdensity, and the MRI a contrast-enhancing tumour arising from the pituitary gland but lying mainly in the suprachiasmatic region, with compression of the third ventricle and the hypothalamus. The differential diagnosis of tumours in the sellar and suprasellar region are pituitary adenomas with or without haemorrhage (apoplexy), meningiomas, thrombosed saccular aneurysms, teratomas, craniopharyngeomas, sarcoidosis, pituitary lymphomas and optic pathway tumours.

The radiological features of this patient, i.e. a cystic lesion in the suprasellar region with calcifications, are highly characteristic of craniopharyngiomas.

Visual field testing and an endocrine work-up in this patient were normal. Treatment consists in the medical management of endocrine dysfunction and surgery with the goal of total resection or a combination of limited surgery and radiotherapy. No treatment decisions have been made in this patient yet.

References

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