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Abstracts

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Die Aphasie als Ausdruck einer Teilleistungsstörung

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Aus der Sicht der Teilsysteme, d.h. von kortikalen Neuronenverbänden, die in einem bestimmten Teil der Grosshirnrinde und für eine bestimmte Teilleistung zuständig sind, erklärt sich die Aphasie als Störung des Sprach-Teilsystems in seiner Interaktion mit dem Globalsystem. Entscheidend bei diesen vernetzten Verbänden sind nicht die Bahnen wie bei den afferenten und efferenten Systemen, sondern die Ansprechbarkeiten der vernetzten Teilsysteme gegenüber dem alles zusammenbauenden Global-system und umgekehrt, woraus sich eine Wechsel-Dynamik nach dem Gesetz der Wechselwirkung ergibt.

Betablockers and riboflavin in prophylactic migraine therapy: differential effects on the intensity dependence of auditory evoked cortical potentials

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Between attacks migraine patients have abnormalities in cortical information processing and in brain mitochondrial energy reserve. Both are most probably relevant for migraine pathogenesis and they could be differentially modified by prophylactic drug therapy. The intensity dependence of the auditory cortical evoked (IDAP) is on average increased in migraine. We have studied IDAP in 26 patients before and after a 4-month prophylaxis with betablockers (n=11, all MO; metoprolol or bisoprolol) or riboflavin (n=15, MO: 13, MA: 2). Recordings were performed as previously described (Proietti Cecchini et al. 1997) at least 3 days before or after an attack.

After the treatment with betablockers IDAP was significantly decreased (before: $1.66 \pm 1.02 \mu\text{V}/10 \text{ dB}$; after: $0.79 \pm 1.06 \mu\text{V}/10 \text{ dB}$; $p=0.02$). The IDAP decrease was significantly correlated with clinical improvement ($r=0.69$, $p=0.02$). There was no change in IDAP after riboflavin treatment (before: $1.80 \pm 0.81 \mu\text{V}/10 \text{ dB}$; after: $1.56 \pm 0.83 \mu\text{V}/10 \text{ dB}$; $p=0.39$), although the majority of patients were improved.

These results confirm that betablockers and riboflavin act on two distinct pathophysiologic mechanisms. Combining both treatments might enhance efficacy without increasing CNS side effects.

Reorganization of cerebral motor systems in multiple sclerosis (MS) measured with positron emission tomography (PET) and F-18 fluoro-deoxyglucose (FDG)

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Background: Transient or persisting motor deficit may significantly contribute to the overall disability of MS patients. Whereas there is considerable evidence for neuronal regeneration at the molecular level, little is known about plasticity within functional, e.g. motor, systems in MS, which can be assessed in vivo by measurement of energy metabolism with PET.

Patients/Methods: Measurement of cerebral glucose metabolism (CMRGlucose) with PET and FDG, 47 MS patients (age 42±9 years, disease duration 12±8 years, n=25 chronic-progressive (CP), n=22 relapsing-remitting (RR)), 19 healthy subjects (CON). Statistical Parametric Mapping, group-to-group comparisons, covariance analysis using total EDSS, pyramidal and cerebellar EDSS subscores.

Results: Compared with CON, patients showed relatively increased CMRGlucose in cortical areas involved in movement preparation (SMA), and relatively decreased CMRGlucose in areas involved in motor control (cerebellum, brain stem) ($p < 0.0005$). This was independent from the clinical course or disease duration. With increasing values of the pyramidal or cerebellar functional system score of the EDSS, CMRGlucose decreased bilaterally in the SMA, fronto-insular and posterior fronto-temporal cortex.

Conclusion: MS patients share brain energy metabolism patterns with patients suffering from spinal cord injury, stroke or ALS. Our data suggest that substantial plasticity occurs within the cerebral motor system in MS.

MRI findings in isolated spinal psammomatous melanotic schwannoma

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A 47-year-old man presented with subacute (over several weeks) monoparesis of the right leg following a three years history of radiating low back pain. Magnetic resonance imaging disclosed an hourglass tumor with unusual signal characteristics (hyperintense on T1-weighted images and hypointense on T2-weighted images). With two laminectomies the tumor could be completely excised. Histology showed a psammomatous melanotic schwannoma without malignant features. The patient exhibited no additional symptoms suggestive of the Carney complex and remains free of symptoms for more than one year. Since more than half of these tumors occur in the setting of the Carney complex with potentially harmful cardiac involvement, correct diagnosis is of relevance.

Radiation-induced carotid vasculopathy: a case-control study using scored Doppler and duplex ultrasound

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Background: Radiation therapy has been shown to accelerate atherosclerosis which may also involve the carotid arteries in the case of neck irradiation.

Methods: Patients irradiated for laryngeal carcinoma (n=60), were examined in a retrospective case control study using Doppler- and duplex ultrasound. The results of Doppler- and duplex investigations were quantified by atheromatosis scores and statistically analyzed.

Results: The atheromatosis scores in the irradiated group were higher than in controls. For the overall score this difference did not reach statistical significance. In the case group, several measure sites showed a significant correlation between the atheromatosis score and a shorter application time of the total dose as well as a larger radiation to examination interval.

Conclusions: Irradiation alone proved an independent risk factor for carotid atherosclerosis when assessed with semiquantitative ultrasound. Therefore follow-up investigations after radiation therapy of the neck are indicated especially in patients with multiple vascular risk factors. Non-invasive semiquantitative Doppler- and duplex-studies are sensitive enough for this purpose.

Chronic progressive primary lumbosacral plexus neuritis: MRI findings and response to immunoglobulin therapy

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A 77-year-old man presented a slowly (over several years) progressive sensorimotor affection of the left leg, which after extensive evaluation finally was attributed to chronic progressive idiopathic lumbosacral plexopathy. Magnetic resonance imaging of the pelvis suggested an inflammatory lesion of the lumbosacral plexus in the clinically corresponding nerve segments (T2-hyperintense lesions, slight enhancement after contrast application). Despite the lack of a biopsy specimen, the long disease course very probably allows the exclusion of a neurolymphomatosis. With intermittent intravenous immunoglobulin therapy partial remission with long term persistence was achieved.

Clinical applications of functional Imaging (MR activation and perfusion studies)

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Today, a variety of clinical questions regarding brain function (activation, perfusion) can not only be assessed with conventional modalities (Doppler, electrophysiology), but also with imaging technologies.

In clinical routine, functional Magnetic Resonance Imaging (fMRI) studies are established as a means to localize primary sensorimotor and language areas in the individual brain in the pre-operative workup even if gross anatomy is changed by, e.g., a space occupying lesion. Our results indicate that this non-invasive technique is as reliable as the Wada test, which involves catheter angiography.

While diffusion imaging is already established for the early assessment of stroke, perfusion imaging (PI) is gaining importance as an additional tool to estimate the extent of an ischemic lesion. In future, a combination of these methods will possibly allow for a more accurate prediction of the clinical outcome.

In addition, PI is beneficial in evaluating both hypoperfusion (e.g. impairment of hemodynamics caused by arterial or venous stenosis or occlusion) and hyperperfusion (e.g. vascular malformation with high shunt volume).

In contrast-enhancing tumors, PI allows to differentiate between excess vascularization and capillary leakage. It remains to be seen whether this method will allow pre-operative visualization of focal areas of higher malignancy within a tumor.

Interface type organotypic cultures of the rat hippocampus – a model for hippocampal epilepsy

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We performed whole-cell patch clamp recordings in CA1 pyramidal neurons in interface type hippocampal cultures. CA1-neurons demonstrated electrophysiological properties similar to CA1 neurons in acute-slice preparations. However, CA1 cells in our preparation showed a remarkably high frequency, of spontaneously occurring synaptic currents at 21.8 Hz at holding potential of -65mV. Among these spontaneously occurring events a subpopulation of large-amplitude events could be distinguished. The peak amplitude of these synaptic currents ranged between 0.5 and up to 3 nA, occurred at 1.12 Hz and were entirely abolished by the selective AMPA-receptor antagonist NBQX (1 mM). The generation of these giant currents was entirely suppressed by the Na⁺ channel blocker TTX (0.5 mM), indicating that they reflected synchronized triggering of AP in a number of pyramidal cells.

Application of the GABA_A-receptor antagonist bicuculline (10 mM) completely blocked inhibitory synaptic transmission, and resulted in a dramatic sequential change of spontaneous synaptic activity. First the huge amplitude events disappeared completely, while medium (100-400 pA) to small size (10-100 pA) synaptic currents remained. These currents were NBQX-sensitive, and had an extremely fast rise and decay time. After 1-5 minutes, these currents become synchronized and occur in bouts of AMPA-receptor mediated synaptic activity lasting 100-200ms. Thereafter these bouts fade and give way to giant synaptic currents at 1.12 ± 0.26 Hz, measuring several nA in magnitude.

These experiments indicate that several categories of spontaneous events can be recorded in organotypic cultures, reflecting the synchronized activity of a defined set of synaptic connections. These synchronizations appear despite normal AMPA, NMDA and GABA_A-receptor mediated synaptic transmission, since quantal size and kinetic properties, as well as synaptic connectivity were identical as compared to other slice preparations. Blockade of inhibition disrupts this activity, leading to the progressive occurrence of giant excitatory currents.

Clinical neuro-oncology: a multidisciplinary approach

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Current standard treatments of patients with malignant gliomas (surgery, radiotherapy) result in an overall survival of 9 to 12 months. Of note subgroups of patients e.g. oligodendroglial tumors may substantially benefit from adjuvant chemotherapy as well as from reoperation. In addition, long-term survivors (up to 5 years) are recognized, suggesting that criteria other than clinical or histological may also determine the prognosis. Therefore, routine investigations may be complemented by molecular biological or physiological measures in tumor and peritumoral edema, which at the moment have not been evaluated in detail. Based upon such data sets patient management has to be optimized individually. To achieve this goal a multidisciplinary team (oncology, neurosurgery, neurology, radiotherapy, molecular pathology) is warranted. We present the concept which is pursued at our hospital.

Static ocular counterroll and three-dimensional dynamic VOR in patients with acute and chronic vestibular paralysis

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We asked whether unilateral vestibular neuritis (VN) causes the same deficits of ocular counterroll during static head roll (OCSR) and dynamic vestibulo-ocular reflex gains during head impulses (VORHI) as unilateral vestibular deafferentation (VD). Five patients with acute and 10 patients with chronic vestibular paralysis after VN were examined. The testing battery included fundus photography of both eyes with the head upright and dual search coil recordings in a three-field magnetic frame. Results were compared with a group of 10 healthy subjects.

Compared to the VD-patients, as reported in the literature, acute VN-patients showed the same pattern of OCSR gain reduction and binocular cyclorotation (CRb). The main feature that distinguished chronic VN-patients from chronic VD-patients was the normalization of the torsional VORHI gain to the affected side. Chronic VN-patients differed from acute VN-patients by: (1) symmetrical OCSR gains, (2) a less pronounced binocular cyclorotation toward the affected side, and (3) a normal torsional VORHI gain toward the affected side. Since this ipsilesional torsional VORHI gain does not recover in VD-patients, the normalization of this gain in our VN-patients can only be explained by a (partial) recovery of otolith function on the side of the lesion after the neuritis.

Semantic processing in the left and right cerebral hemisphere: a brain mapping study

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Behavioural studies using lateralised lexical decision tasks suggest that semantic facilitation is mediated sometimes by the left hemisphere (LH), sometimes by the right hemisphere (RH). The question remains whether different networks are activated in these two presentation conditions. This study was undertaken to identify the electrophysiological correlates of this facilitation and to compare the neural networks involved in the RH and the LH. Multi-channel ERPs were recorded from subjects performing the same categorisation task. ERPs map series averaged separately for visual fields (VFs), semantically related (SR) and unrelated (SU) conditions were segmented into sequences of quasi-stable map configurations. This revealed 7 segments (S1 to S7) in each VF of which S6 and S7 were identical between VF conditions (~400-600ms). Statistical analysis on the duration of these segments showed that S7 was longer in the SU conditions. Finally, source localisation analysis showed that (1) presentation to the RH showed an early callosal transfer of information to the LH at 200ms; (2) S6 and S7 activated the same LH's anterior and postero-temporal regions, suggesting that a common network is engaged when processing semantic categories, independently of the VF. However, the weight of activation of the different areas seem to differ according to visual field.

Changes of brain GABA-levels induced by orally given pyridoxalphosphate measured by proton-magnetic-resonance-spectroscopy

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Gamma-aminobutyric acid (GABA) is synthesized primarily by a single enzyme, glutamate decarboxylase (GAD) which removes the alpha-carboxyl group from the amino acid precursor glutamate. GAD exists in two forms i.e. GAD 65 and GAD 67. Both enzymes need pyridoxal-phosphat (PP) as a co-enzyme. We undertook a study with the aim to determine if it is possible to demonstrate an increase of the GABA-synthesis by orally given PP in healthy subjects in vivo using ¹H-magnetic resonance spectroscopy (¹H-NMR).

Methods: We studied 6 healthy subjects which were divided in three treatment groups with 2 subjects in each. These groups differed in the daily dose of VGB taken during the study. After measurement of baseline GABA-levels in a volume of 8 cm located in right and left occipital lobes, subject A of a treatment group started taking 300 mg PP/d orally for 5 d, subject B took VGB (dose range 1000-3000 mg/d) during the same time. After 5 d the measurements were repeated. Subject A of a treatment group combined then the 300 mg/d PP with the same dose of VGB as subject B took in the previous treatment phase and subject B added 300 mg/d PP to the preexisting regimen with VGB. The last measurements were performed after 5 d of the combined treatment.

Results: After ingesting 300 mg/d PP orally for 5 d, none of the A subjects showed a change of the brain GABA-levels. As expected there was an increase of the brain GABA-levels in all B subjects after taking VGB for 5 d. After 5 d of the intake of VGB and PP together, there was no change of GABA-levels in B subjects and a decrease of GABA-levels to the niveau at baseline in all but one (3000 mg/d) B subjects compared to the GABA-levels during VGB monotherapy.

Conclusion: Despite high doses of PP there was no measurable increase in the GABA-content in the A subjects. In the second treatment phase the combination of PP and VGB led to a decrease of the previously increased GABA-levels of the B subjects and to no significant change of the GABA-levels of the A subjects. This seemingly paradoxical findings will be discussed.

Akuter Meningismus bei ausgedehnter leptomeningealer Metastasierung eines subtotal resezierten high-grade Glioms ohne Lokalrezidiv nach Radiotherapie und unter Chemotherapie

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Einführung: Eine leptomeningeale Metastasierung bei high-grade Gliomen ist bei fortgeschrittenem Krankheitsverlauf keine Rarität. Dass sie frühzeitig auftritt und die klinische Symptomatik prägt (Meningismus, Hydrozephalus, Bewusstseins-trübung) ist selten (2-4%).

Kasuistik: Bei einem 36-jährigen Mann wurde 02/97 ein anaplastisches Astrozytom WHO III temporal rechts subtotal reseziert und 03/97 bis 05/97 mit 60Gy nachbestrahlt. Unter Chemotherapie mit CCNU, Vincristin und Procarbazin seit 05/97 kam es 12/97 zu einem Meningismus und Bewusstseins-trübung. Die Liquoruntersuchung zeigte eine monozytäre Pleozytose ohne Malignitätszeichen, ein stark erhöhtes Eiweiss (7 g/l) und eine erniedrigte Glukose. Trotz Intensivtherapie starb der Patient zirka 8 Wochen nach Beginn der aktuellen Symptomatik und 11 Monate nach der Tumoroperation. Die Autopsie zeigte eine ausgedehnte meningeale Aussaat eines malignen Glioms ohne Hinweis auf ein Lokalrezidiv.

Schlussfolgerung: Die rasante Entwicklung einer Meningeosis neoplastica ist auch bei Gliomen (meist high-grade) möglich. Bemerkenswert bei unserem Patienten ist das Auftreten unter Chemotherapie ohne Hinweis auf ein Lokalrezidiv des 11 Monate zuvor subtotal entfernten Primärtumors.