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11. Jahrestagung

der Österreichischen Gesellschaft für Neurologie

Editorial

Liebe Kolleginnen und Kollegen,

Univ.-Prof. Dr. Mag. Eugen Trinka
Tagungspräsident

ich darf Sie herzlich zur 11. Jahrestagung der Österreichischen Gesellschaft für Neurologie in Salzburg begrüßen!
Es ist uns eine große Ehre und ein Vergnügen, die Tagung in Salzburg ausrichten zu dürfen! Das Programm richtet sich an alle Ärztinnen und Ärzte in Ausbildung sowie an Fachärzte und Fachärztinnen – sowohl im niedergelassenen als auch im Spitalsbereich. Junge Forscherinnen und Forscher haben die Gelegenheit, ihre Arbeiten im Rahmen der Postersitzung, der ausreichend Raum gewidmet wird, zu präsentieren. Mit der Sitzung „What did I learn?" setzen wir eine erfolgreiche Neuerung der Grazer Jahrestagung fort, wobei prominente VertreterInnen der österreichischen Neurologie die besten wissenschaftlichen Arbeiten der Tagung ins Licht setzen.

Einen Themenschwerpunkt stellen die Epilepsien dar, deren Bedeutung durch die „Written Declaration on Epilepsy" (EU-Parlament 022/214) und die darauffolgende Ausrichtung des FP7-Forschungsprogramms mit dem Fokus auf Epileptogenese und antiepileptogenetische Therapien besondere Bedeutung bekommen hat.
Ein weiterer Themenschwerpunkt sind die neuroimmunologischen Erkrankungen. Neuroimmunologische Prozesse spielen nicht nur bei der Multiplen Sklerose und bei Autoimmunenzephalitiden unter immunmediierten Neuropathien eine Rolle, sondern sind auch in den Blickpunkt anderer Themengebiete gerückt, was sich auch in neuen und innovativen Therapieansätzen zeigt. Die Fortschritte in ausgewählten Bereichen der Neurologie werden im „Presidential Symposium" mit international herausragenden ReferentInnen vertieft.

Den weiteren Themenschwerpunkten zerebrovaskuläre Erkrankungen, Neurorehabilitation sowie Neuroonkologie wird in der Tagung ebenfalls Raum gewidmet.
Die Fortbildungsakademie soll mit einem neuen, straffen Programm den Grundstein zu einer erfolgreichen postgraduellen, kontinuierlichen Aus- und Weiterbildung setzen, die in Zukunft zunehmend an Bedeutung für die Weiterentwicklung des Faches, vor allem im niedergelassenen Bereich und bei den praktisch tätigen Kolleginnen und Kollegen haben wird.

Die Organisation der Tagung und die Auswahl der Themen wurden tatkräftig durch den Vorstand der ÖGN sowie das ÖGN-Sekretariat unterstützt. Ich möchte auf diesem Weg besonders die unermüdliche Arbeit von Frau Tanja Weinhart hervorheben, ohne die es nicht gelungen wäre, in Zeiten wirtschaftlicher Restriktionen die Tagung auch ökonomisch erfolgreich durchzuführen.

Ich möchte mich in diesem Zusammenhang auch für die hervorragende Zusammenarbeit mit den PartnerInnen aus der Industrie bedanken, die sowohl bei der Themenwahl der Satellitensymposien immer Bezug auf das Hauptprogramm genommen haben als auch mit der Industrieausstellung einen ganz wesentlichen Beitrag zur erfolgreichen Gestaltung der Tagung liefern.

Anlässlich dieses Sonderbandes der Zeitschrift ***neurologisch*** möchte ich mich bei den Gründungschefredakteuren Bruno Mamoli und Regina Katzenschlager bedanken, die diese Initiative einer eigenen neurologischen Fachzeitschrift der Österreichischen Gesellschaft für Neurologie gestartet haben, deren Erfolg über jeden Zweifel erhaben ist und die nun von Dr. Ackerl gemeinsam mit Prof. Mamoli fortgesetzt wird. Dazu hat auch die Arbeit von Frau Natascha Fial ganz wesentlich beigetragen, bei der ich mich auf diesem Wege für die langjährige Zusammenarbeit bedanken möchte!

Nicht zuletzt gilt mein Dank Priv.-Doz. Regina Katzenschlager und Prof. Bruno Mamoli sowie dem ÖGN-Vorstand, die Universitätsklinik für Neurologie in Salzburg mit der Organisation der Tagung zu betrauen. Die MitarbeiterInnen der Klinik, insbesondere das lokale Organisationskomitee, haben durch ihren Einsatz ebenfalls einen großen Beitrag zum Gelingen dieser Jahrestagung geleistet.

Univ.-Prof. Dr. Mag. Eugen Trinka

Inhalt Abstractband

IMPRESSUM **Herausgeber:** Österreichische Gesellschaft für Neurologie, Univ.-Prof. Dr. Eduard Auff, Präsident der ÖGN. **Chefredaktion:** Univ.-Prof. Dr. Bruno Mamoli, Priv.-Doz. Dr. Regina Katzenschlager. **Medieninhaber und Verlag:** MEDMEDIA Verlag und Mediaservice Ges.m.b.H, Seidengasse 9/Top 1.1, A-1070 Wien, Tel.: 01/407 31 11-0, E-Mail: office@medmedia.at. **Verlagsleitung:** Mag. Gabriele Jerlich. **Lektorat:** onlinelektorat@aon.at. **Layout/DTP:** Martin Grill. **Projektbetreuung:** Natascha Fial. **Coverfotos:** Tourismus Salzburg, Salzburg Congress. **Print:** Donau Forum Druck Ges.m.b.H., Wien. **Bezugsbedingungen:** Die Zeitschrift ist zum Einzelpreis von Euro 9,50 plus MwSt. zu beziehen. **Grundsätze und Ziele von neurologisch:** Kontinuierliche medizinische Fortbildung für Neurologen, Psychiater und Allgemeinmediziner. **Allgemeine Hinweise:** Namentlich gekennzeichnete Beiträge geben die persönliche und/oder wissenschaftliche Meinung des jeweiligen Autors wieder und fallen somit in den persönlichen Verantwortungsbereich des Verfassers. Angaben über Dosierungen, Applikationsformen und Indikationen von pharmazeutischen Spezialitäten müssen vom jeweiligen Anwender auf ihre Richtigkeit überprüft werden. Trotz sorgfältiger Prüfung übernehmen Medieninhaber und Herausgeber keinerlei Haftung für drucktechnische und inhaltliche Fehler.

Bewegungsstörungen

A 01 Supine hypertension in Parkinson's disease and in multiple system atrophy: final analysis of a large retrospective cohort

Fanciulli A.[1, 2], Göbel G.[3], Ndayisaba J. P.[2], Granata R.[2], Dürr S.[2], Strano St.[4], Colosimo C.[5], Poewe W.[2], Pontieri F. E.[1, 6], Wenning G. K.[2]

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Background: Cardiovascular autonomic failure is a frequent non-motor feature of Parkinson's disease (PD) and multiple system atrophy (MSA). Beyond orthostatic hypotension (OH), supine hypertension (SH) may develop and possibly exert a negative role on survival, cerebrovascular and cognitive outcome in parkinsonian syndromes. However, the actual prevalence of SH diagnosed according to the most recent international criteria, up to date, has never been investigated in parkinsonian syndromes.

Objective: Primary endpoints of the present study were to investigate the prevalence and severity of SH in a retrospective cohort of PD and MSA patients. Secondary endpoints were: 1) to assess any difference in the prevalence and/or severity of SH in the parkinsonian (MSA-P) versus the cerebellar (MSA-C) variant of MSA; 2) to assess any difference in the prevalence and/or severity of SH in a cohort of PD-Dementia (PDD) cases with respect to gender-, age- and disease duration- matched PD cases; 3) to assess the clinical and tilt test correlates of SH in PD and MSA.

Methods: 197 PD (164 PD, 33 PDD) and 78 MSA (24 MSA-C, 54 MSA-P) patients were included in the present study. Cardiovascular autonomic function was evaluated in a standardized setting by means of continuous ECG and non-invasive beat-to-beat blood pressure (BP) monitoring (Task Force™ Monitor, CNSystems). Supine BP was evaluated after 10 minutes in the lying position and orthostatic BP changes were evaluated for 10 minutes after 60° passive head-up tilting and for 5 minutes during active standing.

Results: SH (>140 mmHg systolic, >90 mmHg diastolic) was observed in 34 % and 37 % of PD and MSA patients, respectively. In PD, SH was mild in 71 % of cases, moderate in 27 % and severe in 2 %, while in MSA SH was mild in 55 % of patients, moderate in 17 % and severe in 28 % ($p=0.004$). No difference was observed in the prevalence of SH between the MSA-P and MSA-C cohort, but MSA-P patients showed a trend towards more severe degrees of SH ($p=0.045$). The PD and PDD cohort showed no difference in the prevalence or severity of SH. No association was observed between SH and sex, age, disease duration or H&Y stage either in PD or in MSA. Regression analysis showed an association between SH and cardiovascular comorbidities ($p<0.001$) in PD and with the presence of OH ($p=0.002$), use of anti-hypertensive medications ($p=0.039$) and lower daily dopaminergic intake ($p=0.011$) in MSA. SH was associated with greater systolic ($p=0.007$) and diastolic ($p=0.002$) BP fall during both head-up tilt and active standing in PD.

Conclusions: Our results show that one third of PD and MSA patients may suffer from mild to severe SH, independent from age, disease duration or severity. In PD, cardiovascular comorbidities may significantly contribute to the development of SH, while in MSA, SH may more stringently depend upon cardiovascular autonomic failure. Phase III clinical trials investigating potential neuroprotective effects from Calcium antagonists of the dihydropyridine class in PD are currently underway. If replicated in future studies, short-acting Calcium antagonists may represent the therapy of choice to achieve antihypertensive effects in parkinsonian syndromes.

A 02 Validation of „laboratory-supported" criteria for functional tremor

Schwingenschuh P.[1], Saifee T. A.[2], Katschnig-Winter P.[1], Kögl-Wallner M.[1], Macerollo A.[2], Culea V.[1], Ghadery C.[1], Pendl T.[1], Seiler S.[1], Werner U.[1], Hofer E.[1], Maurits N.[3], Tijssen M. A.[3], Schmidt R.[1], Bhatia K. P.[2], Edwards M. J.[2]

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Objective: To validate an electrophysiological test battery as a tool to diagnose patients with functional tremor (FT) based on a "laboratory-supported" level of certainty.

Background: In a small group of patients, we have previously shown that a combination of electrophysiological tests with a cut-off score of 3/10 points was able to distinguish FT and organic tremor (OT) with excellent sensitivity and specificity. A validation of this test battery is warranted before advising its use in clinical practice.

Methods: Based on the results of power calculations, we prospectively recruited 40 patients with FT (mean age 37.3±24.7 years; mean disease duration 5.7±8.9 years) and 72 patients with OT (mean age 56.1±24.7 years; mean disease duration 16.1±17.8 years). Tremor was recorded at rest, posture (with and without loading), and action, while performing tapping tasks (1, 3, 5 Hz), and while performing ballistic movements with the less affected hand. Analyses were performed, as previously described (1), by raters blinded to the clinical diagnosis. A subset of recordings was analyzed by three blinded raters and a subgroup of patients was tested twice on different days.

Results: Patients with FT had a higher average score on the test battery, compared to the patients with OT (3.5±1.5 points versus 1.0±0.8 points; P<0.001). The predefined cut-off score for a diagnosis of laboratory-supported FT with 3 out of 10 points yielded a test sensitivity of 85.0 % and a specificity of 95.8 %; P<0.001. We demonstrated a good interrater-reliability and test-retest-reliability.

Conclusions: We propose this test battery as the basis of laboratory-supported criteria for the diagnosis of functional tremor and we now encourage its use in the work-up of patients with presumed FT.

[1] Schwingenschuh P., Katschnig P., Seiler S., Saifee T. A., Aguirregomozcorta M., Cordivari C., Schmidt R., Rothwell J.C., Bhatia K. P., Edwards M. J. Moving toward "laboratory-supported" criteria for psychogenic tremor. Mov Disord 2011 Dec; 26(14):2509–15

A 03 Extending the phenotype of transgenic MSA: presence of hα-syn in PNS: an update

Kuzdas-Wood D.[1], Malsch P.[2], Theurl M.[3], Mair N.[2], Irschick R.[4], Wanschitz J.[1], Kress M.[2], Klimaschewski L.[4], Poewe W.[1], Stefanova N.[1], Wenning G. K.[1]

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Objective: To evaluate the relevance of human hα-syn positive aggregates in the peripheral nervous system (PNS) of the PLP hα-syn mouse model of multiple system atrophy (MSA) using different methodological approaches.

Background: Detailed characterization of animal models is of great importance for unraveling pathogenic mechanisms in MSA research. The CNS of the PLP hα-syn MSA mouse model has been well-characterized in previous studies. It displays specific expression of hα-syn restricted to oligodendrocytes. Since the expression of hα-syn is under control of the PLP promoter, hα-syn is also present in the Schwann cells of this model. Peripheral neuropathy has been reported in 30 % of MSA patients, the cause remaining

unclear; however, it may be connected to the presence of α-syn in the PNS of these patients.

Methods: Hα-syn positive aggregates were detected in sciatic nerve sections of the MSA model by immunohistochemistry. Motor ability, mechanical and heat/cold sensitivity tests and electrophysiological experiments were performed to analyze whether the peripheral α-syn pathology of this MSA mouse model leads to altered sensitivity, pain sensation or altered nerve conductance properties over a time-course of seven months. Nerve conductance velocity was measured in vivo and ex vivo.

Results: Hα-syn was detected in Schwann cells of the sciatic nerve of the MSA mouse model. Comparison of age-matched healthy control mice with the transgenic MSA mice revealed increased heat/cold sensitivity in the MSA group. Nerve conductance measurements as well as analysis of the myelin sheaths thickness and investigation of thermosensitive ion channels TRPA1 and TRPM8 did not reveal significant differences between the groups.

Conclusions: Hα-syn is present in the PNS of transgenic MSA mice and is associated with increased heat/cold sensitivity. Nerve conductance velocity, thickness of the myelin sheaths and heat/cold channel expression did not differ between transgenic MSA mice and an age-matched healthy control group indicating a more central origin of disturbed heat/cold sensation.

A 04

Mechanisms of alpha-synuclein oligodendroglial cytoplasmic inclusion formation – in vitro evidence

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Background: Multiple system atrophy (MSA) is a progressive, fatal, neurodegenerative disorder of unknown etiology. Glial cytoplasmic inclusions (GCIs) in oligodendroglial cells are the pathological hallmark of MSA. The presence of GCIs, throughout the brain, is associated with progressive neuronal loss as well as glial activation. The main component of GCIs is the neuronal protein α-synuclein (AS). A possible mechanism of AS positive inclusion formation in oligodendroglial cells in MSA is cell-to-cell propagation of AS. Furthermore, the formation of intracytoplasmic AS aggregation may be caused by an impairment of AS degradation or uptake by oligodendroglial cells.

Objective: The aim of the current study is to identify mechanisms that play a role in the accumulation of AS in oligodendroglial cells in vitro.

Methods: Experiments were performed using the human oligodendroglial cell line MO 3.13 as a model system. The uptake of recombinant soluble AS was investigated using immunocytochemistry and western blot. In an attempt to trigger intracellular accumulation of AS, AS degradation was blocked by the autophagy blocker bafilomycin A1 and 3-methyladenine or cytoskeletal disruption was induced using nocodazole and vascular endothelial growth factor alpha (VEGF-A).

Results: Treatment with bafilomycin A1 and VEGF-A revealed an increased number of cells with intracytoplasmic AS. Moreover, the number of inclusion per cell was significantly augmented upon bafilomycin A1 treatment. Nocodazole treatment with 100 ng/ml induced an enhanced total area of inclusions per cell. No effect was found in cells exposed to 3-methyladenine and AS.

Conclusion: These preliminary data indicate that blocked fusion of autophagosome with lysosome (bafilomycin A1) and disruption of the actin cytoskeleton (VEGF-A) may enhance the number of cells with AS positive inclusions. In addition, the disruption of microtubules through nocodazole treatment may induce an enhanced aggregation of AS per cell. Further experiments are needed to identify the mechanisms of GCI formation which may provide novel insights into the pathogenesis of MSA.

Acknowledgements: This study is supported by a grant of the Austrian Science Funds (FWF) P25161.

A 05

HDAC inhibition by sodium phenylbutyrate protects catecholaminergic neurons in a transgenic mouse model of multiple system atrophy: implications for therapy

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The aim of the current study is to analyze the effects of histone deacetylase (HDAC) inhibition as a candidate neuroprotective strategy in a transgenic mouse model of multiple system atrophy (MSA), a fatal atypical parkinsonian disorder associated with oligodendroglial alpha-synuclein inclusions.
Within the last years, HDACs have been implicated to play an important role in the pathogenesis of neurodegenerative diseases. It has been shown that their inhibition protects neurons in models of Parkinson's disease (Roy A. et al., 2012) and amyotrophic lateral sclerosis (Cudkowicz M. E. et al., 2009). We here address the neuroprotective efficacy of sodium phenylbutyrate (NaPB), a non-selective pan-HDAC inhibitor, in a transgenic mouse model of MSA.
Daily intra-peritoneal injections of NaPB or saline were applied over a period of two months in PLP-alpha-synuclein transgenic MSA mice, overexpressing human alpha-synuclein in oligodendroglia. Behavioral tests were performed to assess progression of motor deficits. Immunohistochemistry and biochemical analysis were applied to identify the effects of NaPB treatment in selected neurodegenerating regions of the MSA brain. So far, immunohistochemistry showed that the application of NaPB has a neuroprotective effect on dopaminergic neurons in substantia nigra pars compacta and noradrenergic neurons in locus coeruleus of MSA mice.
Our preliminary data suggest that the pan-HDAC-inhibitor NaPB has a neuroprotective effect on nigral dopaminergic neurons and noradrenergic neurons in locus coeruleus of transgenic MSA mice. Epigenetic mechanisms including histone modifications should be investigated further as potential targets in MSA therapy.

Acknowledgement: This study is supported by grants of the Austrian Science Funds (FWF) F4404 and P25161. We also thank Karin Spiss for her excellent technical assistance.

A 06

Gibt es polysomnografische Charakteristika der Augmentation beim Restless-Legs-Syndrom?

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Hintergrund/Ziel: Die Augmentation des Restless-Legs-Syndroms (RLS) ist eine potenziell schwerwiegende Nebenwirkung dopaminerger Therapie. Die Hauptmerkmale sind eine Verschlechterung der RLS-Beschwerden mit einer Vorverlagerung der Symptomatik zu früheren Tageszeiten, einer kürzeren Symptomlatenz in Ruhe und häufig eine Ausbreitung der Symptome auf andere Körperteile. In der Literatur gibt es bisher kaum Daten zur motorischen Aktivität bei Augmentation. Das Ziel der vorliegenden Studie war es, detailliert die motorische Aktivität bei augmentierten RLS-Patienten zu untersuchen und mit nichtaugmentierten RLS-Patienten zu vergleichen.
Methoden: Bei 45 Patienten mit idiopathischem RLS (15 untherapiert, 15 therapiert [nichtaugmentiert], 15 augmentiert) erfolgte eine Videopolysomnografie mit erweiterter EMG-Montage, ein Suggested Immobilization Test (SIT) und ein RLS-Schweregrad-Assessment (IRLS, RLS-6 Skalen, CGI item 1 und ASRS).
Resultate: Die Indices der periodischen Beinbewegungen (PLM) im Schlaf- und Wachzustand wie auch der Periodizitätsindex (PI) und das Muskel-Rekrutierungsmuster unterschieden sich nicht zwischen den 3 Gruppen ($p > 0,05$). Die ultradiane Verteilung im Nachtverlauf der PLM im Schlaf erbrach-

te signifikante Unterschiede in der 2. und 3. Stunde Schlaf ($p < 0,05$). Im SIT hatten augmentierte RLS-Patienten eine Tendenz zu den höchsten PLM-Indices (Median/Range augmentiert vs. therapiert [nichtaugmentiert] vs. untherapiert: 62/0–178 vs. 0/0–175 vs. 0/0–191; $p = 0,055$) und auch bei RLS-Schweregradskalen hatten augmentierte Patienten die höchsten Werte (Median/Range augmentiert vs. therapiert [nichtaugmentiert] vs. untherapiert: IRLS: 29/18–39 vs. 11/0–32 vs. 19/0–33; RLS-6: 36/7–52 vs. 14/0–23 vs. 22/0–43; Modus/Range CGI: 6/4–6 vs. 3/2–5 vs. 4/1–5; ASRS item 4 score: 3/1–4 vs. 1/0–3 vs. 2/0–4; alle $p < 0,05$).

Konklusion: Mit dieser Studie konnte gezeigt werden, dass die Polysomnografie in der Diagnosestellung und Evaluierung der Augmentation nur von eingeschränkter Bedeutung ist. Der SIT zeigte grenzwertige Unterschiede bei PLM. Die Unterschiede bei den subjektiven Schweregradskalen waren hingegen deutlich. Somit ist zu folgern, dass sich die Augmentation des RLS vor allem im Wachzustand manifestiert und zu einer deutlichen subjektiven Beeinträchtigung führt.

Diese Studie wurde unterstützt vom Jubiläumsfonds Österreichische Nationalbank (Projekt 12594).

A 07

Effects of the late start of MPO inhibition in a preclinical model of multiple system atrophy

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Background: Multiple system atrophy (MSA) is the most common atypical parkinsonian disorder. Compared to idiopathic Parkinson's disease (PD) it has a more rapid progression of motor disability combined with poor levodopa response and reduced life expectancy. The limited therapeutic options and the rapid deterioration determine a new area of need for developing disease modifying strategies (DMS). Myeloperoxidase (MPO) is a microglial enzyme that has been linked to neurodegeneration owing to its ability to induce oxidative stress. It has been demonstrated that in the MSA mouse model early start of therapy with a MPO inhibitor (MPOi) reduces motor disability and results in preservation of neurons (Stefanova et al., 2012).
Aim: The aimed current study to assess the neuroprotective potency of the late start of MPOi therapy paradigm relevant to the human condition.

Materials and methods: Transgenic PLP-α-synuclein mice aged 9 months were divided into two experimental groups: MSA+vehicle and MSA+MPOi. All animals underwent the low dose 3-nitropropionic acid (3-NP) intoxication in order to replicate the MSA of neuropathology (Stefanova et al., 2005). After inducing full-blown MSA pathology, mice continued receiving either MPOi or vehicle over a period of 20 days. Motor behavior was assessed by clinical motor scale (CMS) evaluation, stride length test and open field activity test. Neuropathology was analyzed in the striatum, substantia nigra pars compacta (SNc), cerebellar cortex (Purkinje cells), pontine nuclei and inferior olives using immunohistochemistry. Statistical analyses were performed according to the distribution of variances either using T-Test for parametric data or using Mann-Whitney Test for non-parametric data.

Results: No motor improvement related to MPOi treatment was detected. The histological investigations revealed a trend towards reduced neuronal loss in the striatum and the SNc, accompanied by a significant reduction of microglia activation in SNc and to a smaller extend in the striatum in the MSA-MPOi group.
Discussion: This study describes the outcome of the late start of therapy with MPOi after induction of full-blown neuropathology via 3-NP application in a transgenic mouse model of MSA. Despite the limited behavioral effects of treatment, the histological investigations support the anti-neuroinflammatory efficacy of MPOi with a tendency of neuroprotection.
Acknowledgements: This study was supported by Astra Zeneca.

A 08

Structural MRI of the cervical spine in patients with cervical dystonia

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Introduction: Cervical dystonia represents the most common form of adult-onset focal dystonia. In this study we used MRI to investigate, if structural changes of the cervical spine are more frequent in patients with cervical dystonia compared to healthy controls and which clinical parameters correlate with these abnormalities. Finally, we investigated whether there are any clinical parameters which strengthen the indication for an MRI of the cervical spine in those patients.

Methods: We recruited 30 consecutive patients (8 men, 22 women) with cervical dystonia. Three months apart, two identical examinations were performed including medical history, a neurological examination, and the evaluation of the cervical dystonia by means of three different rating scales (TSUI Score, Toronto Western Spasmodic Torticollis Rating Scale, Burke-Fahn-Marsden Scale). During the same period, an MRI of the cervical spine was performed, which was analyzed by three experienced neuroradiologists with the help of different MRI rating scales (Kang, Matsumoto, Modic). For comparison, 21 age-matched healthy participants were recruited, who also underwent the above mentioned examination and an MRI of the cervical spine.

Results: The inter-rater reliability of each MRI rating scale revealed good results indicating good reliability of the used scales. We found no significant differences between patients and healthy participants regarding structural changes of the cervical spine. Structural changes in patients with cervical dystonia were associated with several clinical parameters predominantly in segments C3/C4 and C4/C5. However, the clinical relevance of these associations is debatable. Interestingly, the clinical symptom pain was not associated with imaging changes.

Conclusion: Based on our results, there is no indication for routine MRI of the cervical spine in patients with cervical dystonia, since degenerative changes are comparable in patients and healthy controls. An MRI of the cervical spine should therefore only be ordered if clinical signs or symptoms of a cervical radiculopathy, excessive pain, spinal cord abnormality, or spinal stenosis are present. If patients with cervical dystonia are more prone to develop degenerative changes in segments C3/4 and C4/5 – in contrast to non-dystonia patients in whom structural changes are usually predominantly found in lower segments – needs to be further investigated.

A 09 Verletzungsmuster von Parkinson-Patienten nach Stürzen im öffentlichen Bereich

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Hintergrund: Parkinson-Patienten haben aufgrund ihrer Erkrankung motorische Defizite. Daher neigen diese Personen zu Stürzen, vor allem, weil im öffentlichen Bereich nicht so optimale Vorsichtsmaßnahmen gelten, wie vielleicht zu Hause. Allerdings gibt es keine ausreichenden Untersuchungen über Verletzungsmuster und Verletzungsfolgen an Parkinson-Patienten.
Fragestellung: Zweck der Studie war es, bei Parkinson-Patienten Verletzungsmuster sowie Schweregrad und demografische Risikofaktoren bei Stürzen in öffentlicher Umgebung zu untersuchen.
Methode: Retrospektive Erhebung des Krankheitsverlaufes von im öffentlichen Bereich gestürzten, unfallchirurgisch stationär aufgenommenen Parkinson-Patienten über einen Zeitraum von 7 Jahren am Universitätsklinikum Graz. Die Verletzungen wurden nach Körperregionen gegliedert und die Verletzungsschwere nach dem Injury Severity Score (ISS), der Anzahl der Behandlungstage, Operationsbedarf, Intensivpflichtigkeit und dem Outcome bewertet.
Ergebnisse: Innerhalb des Untersuchungszeitraumes mussten 70 Parkinson-Patienten nach Stürzen im öffentlichen Bereich aufgenommen werden. Diese waren überwiegend weiblichen Geschlechts (65,7 %) und fortgeschrittenen Alters (82,14 ± 7,3 Jahre). Verletzungen betrafen hauptsächlich die unteren Extremitäten (78,6 %). Der Rest des Körpers war weniger stark betroffen. Im Detail fanden sich Verletzungen am Kopf in 20 %, an den oberen Extremitäten in 15,7 % und am Rumpf in nur 10 % der Fälle. 27 Patienten (38,5 %) hatten ausgeprägte Verletzungen (ISS > 10), 54 (77,1 %) mussten operativ versorgt werden und 3 Patienten hatten einen letalen Krankheitsverlauf. Das Geschlecht korrelierte mit schwereren Verletzungen ($p = 0,027$), wobei männliche Pati- enten stärker betroffen waren. Das Alter korreliert zwar nicht signifikant mit schweren Verletzungen, jedoch zeigt sich ein Trend ($p = 0,064$).
Zusammenfassung: Da Parkinson-Patienten im öffentlichen Bereich in nicht unbeträchtlicher Anzahl schwere Stürze mit oftmals ausgeprägten Folgen erleiden, sollten gerade für diese Gruppe sturzpräventive Maßnahmen noch stärker Berücksichtigung finden.

A 10 Effects of high altitude exposure on physiological tremor

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Introduction: Various neurological symptoms can occur after an ascent to altitudes higher than 2500 to 3000 meters. Data on the effect of high altitudes on tremor are scarce. One study investigating tremor during exposure to a simulated altitude of 4500 meters showed increased amplitude of physiological tremor. So far, no data exist on the effects of high altitude on physiological tremor under natural conditions.
Methods: One female and five male healthy non-professional mountaineers undertook an expedition to Cho Oyu (peak altitude 8201 m) in Nepal, which represents the sixth highest mountain in the world. We used a smartphone triaxial accelerometer to record postural tremor at 3400 m, 5700m, and 7100 m height after a minimum acclimatization time of 12 hours. Tremor peak frequency and total power as a measure of amplitude were calculated using offline fast

Fourier transformation to derive power spectral analyses.
In addition, blood oxygen saturation (measured non-invasively), heart rate, and the Lake Louise Score (LLS) for Acute Mountain Sickness (AMS) were assessed at all three heights. The LLS is a scoring system that helps make the clinical diagnosis of AMS and includes five self-reported questions regarding the presence of headache, gastrointestinal symptoms, fatigue/weakness, dizziness/lightheadedness, and difficulties with sleeping.

Results: At an altitude of 3400 m mean peak frequency of postural tremor was 5.0 Hz and mean tremor amplitude was 0.001 milliG. After ascent to 5700 m (camp 1) peak tremor frequency decreased to 3.3 Hz and tremor amplitude increased to 0.002 milliG. Three participants reached camp 2 (7100 m). Tremor frequency was 4.2 Hz and tremor amplitude further increased to 0.003 milliG. This increase in tremor amplitude was accompanied by a decrease in average blood oxygen saturation (93 %; 82 %; 74 %), an increase in mean heart rate (65; 83; 85 beats per minute), and worsening of the average LLS score (0; 2; 5) (values for 3400 m; 5700 m; 7100 m).
Conclusion: Under natural conditions in high altitude – and therefore exposure to hypoxia – a significant increase of the amplitude of physiological tremor was found. This effect of hypoxia may result from a cascade of events starting with the activation of the hypothalamic-pituitary-adrenal axis causing elevated catecholamine levels, leading to an enhanced physiological tremor paralleled by raised heart rate.

A 11

Welche Verkehrsmodi sind besonders gefährdend für Parkinson-PatientInnen?

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Hintergrund: Parkinson-PatientInnen sind aufgrund ihrer vielschichtigen motorischen und nichtmotorischen Symptome besonders gefährdet, an Verkehrsunfällen (VU) beteiligt zu sein. Der Fokus der bisherigen Studien lag dabei nahezu ausschließlich auf VU mit Kraftfahrzeugen und daher ist wenig über VU von Parkinson-PatientInnen mit anderen Verkehrsmodi bekannt.
Fragestellung: Zweck der Studie war es, bei Parkinson-PatientInnen die Häufigkeit von stattgefundenen Verkehrsunfällen mit schweren Körperverletzungen herauszufinden und dabei zu eruieren, mit welchen Verkehrsmitteln diese Unfälle verursacht wurden.
Methode: Retrospektive Erhebung des Krankheitsverlaufes von verunfallten, unfallchirurgisch stationär über einen Zeitraum von 10 Jahren am Universitätsklinikum Graz aufgenommenen Parkinson-PatientInnen und alters- und geschlechtsgematchten KontrollpatientInnen.
Ergebnisse: Innerhalb des Untersuchungszeitraumes mussten 18 Parkinson-PatientInnen nach einem VU stationär aufgenommen werden. Diese waren überwiegend männlichen Geschlechts (72,22 %) und fortgeschrittenen Alters (75,28 ± 7,75 Jahre). Der Anteil der VU-bedingten Verletzungen, die im Untersuchungszeitraum zu einer stationären Aufnahme an der Unfallchirurgie führten, ist bei IPS-PatientInnen signifikant größer als derjenige in der Kontrollgruppe (IPS = 2,5 % vs. Ko = 0,6 %; Chi^2 = 41,732; $p < 0,001$). Es besteht im Vergleich zur Kontrollgruppe ein besonders hoher Anteil an in öffentlichen Verkehrsmitteln verletzten IPS-PatientInnen (IPS = 25 % vs. Ko = 6 %; Chi^2 = 7,215; p = 0,057).
Zusammenfassung: Da Parkinson-PatientInnen signifikant häufiger an schweren VU beteiligt sind als andere Populationsgruppen im selben Alter, und hier vor allem bei der Benützung öffentlicher Verkehrsmittel, sollte die wissenschaftliche Untersuchung auf alle Verkehrsmodi ausgedehnt werden. Das Ziel wäre, sicherheitserhöhende Maßnahmen für alle Verkehrsmodi, nicht nur für private Kraftfahrzeuge, zu entwickeln, um Parkinson-PatientInnen die Möglichkeit zu geben, möglichst lange unfallfrei aktiv am Verkehr teilnehmen zu können.

A 12 Treatment of tremor in FXTAS

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Background: Fragile X-associated tremor/ataxia syndrome (FXTAS) is a late-onset neuropsychiatric degenerative disorder predominantly in male FMR1 premutation carriers. Core clinical features include progressive kinetic tremor and cerebellar ataxia. Therapy for tremor is symptomatic and based on expert opinion. Oral medication used for essential tremor (ET) is suggested and so far three patients who underwent deep brain stimulation (DBS) have been reported in the literature.
Objective: To report a patient with FXTAS and disabling arm tremor who underwent DBS.
Methods: A 52 years old man presented in 2011 with saccadic eye movements, rest, action and intention tremor of the upper limbs, mild slowing in finger-tapping, absent lower limbs reflexes and mild gait ataxia. His FMR1 gene showed 120 CGG repeats, FXTAS was diagnosed. Tremor of the upper limbs progressed without lasting benefit to any tried antitremulous medication including propranolol, primidone and gabapentin. Topiramat has not been tried out because of its possibility to cause depression. Therefore, DBS of the zona incerta was performed in December 2012. Postoperatively, the patient showed only mild action tremor of the arms, and he regained independence in activities of daily living (drinking, eating, writing …). During the following months gait ataxia slowly progressed and a walker was needed. In October 2013 the arm tremor worsened again. ON-Stimulation the patient showed a moderate postural and action tremor of both arms, OFF-Stimulation there was a mild head tremor, moderate rest and postural and severe action tremor of the arms. Furthermore, a severe trunk tremor made stance and gait impossible. Therefore, DBS was still considered being effective, but the underlying disease has progressed. Add-on therapy with clozapine (50 mg/day) reduced the arm tremor significantly.
Conclusion: Tremor in FXTAS usually progresses slowly and can be very disabling. Response to oral medication used for ET might be inefficient. Tremor in FXTAS can be improved with DBS of the zona incerta, however progression of tremor and gait ataxia have to be expected as part of the natural disease course. Clozapine may be helpful as add-on therapy. Data on long-time follow-up of FXTAS patients who underwent DBS are currently not available. Controlled trials investigating the therapeutic options in FXTAS patients are warranted.

A 13 Skalen zur Untersuchung von Wearing-off-Symptomen beim Parkinson-Syndrom: eine quantitative Analyse

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Hintergrund: Wearing-off (WO), der oft stark lebensqualitätsbeeinträchtigende vorzeitige Wirkungsverlust der Parkinson-Medikation, tritt in der Mehrzahl der Patienten mit idiopathischem Parkinson-Syndrom nach wenigen Jahren dopaminerger Therapie auf. Zur Evaluierung des WO sind Skalen unabdingbar. Bisherige Empfehlungen zur Auswahl der geeigneten, aus einer Vielzahl von zur Verfügung stehenden WO-Skalen basierten ausschließlich auf klinimetrischen Kriterien, dabei wurde allerdings die Frage der einfachen Anwendbarkeit und damit verbunden der Akzeptanz und daraus folgend der Vergleichbarkeit zu bestehenden Daten nicht berücksichtigt.
Fragestellung: Welche Skalen finden in klinischen Studien zur Untersuchung des WO besonders häufig Verwendung, gibt es eine Veränderung der Präferenzierung im Zeitverlauf und vor allem, was ist dabei der Stellenwert der von der Fachgesellschaft empfohlenen WO-Skalen?
Methode: In einer systematischen Literaturrecherche mit Hilfe der Datenbank „PubMed" wurden alle klinischen Studien über „Parkinson disease" bis 15. 9. 2013 identifiziert und

hinsichtlich der Verwendung von klinischen Skalen und besonders der spezifischen Teile des UPDRS 3.0 und MDS-UPDRS analysiert.
Ergebnisse: Insgesamt wurden 23 WO-Studien, davon 95 % aus den letzten 10 Jahren identifiziert. UPDRS 3.0 war mit Abstand die am häufigsten verwendete Skala (43 %) gefolgt von 9 Item Wearing-Off Quest (21 %), 19 Item Wearing-Off Quest (13,04 %) und der Treatment Response Scale (13,04 %). Der MDS-UPDRS IV kam niemals zur Anwendung. Beim direkten Vergleich der WO-Skalen nach Empfehlungsstatus fiel auf, dass die Skalen mit dem stärksten Empfehlungscharakter seltener verwendet wurden, als jene mit dem zweitstärksten.
Zusammenfassung: Bei der Auswahl von Skalen zur wissenschaftlichen, aber auch klinischen Untersuchung des WO sollten neben qualitativen vermehrt auch quantitative Kriterien Berücksichtigung finden. Wenn Wert auf Vergleichbarkeit mit anderen Daten gelegt werden soll, ist man mit dem UPDRS 3.0 am besten beraten.

Demenz

A 14 *Olfactory bulb pathology in neurodegenerative diseases*

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Objectives: Olfactory dysfunction is a common and early symptom of many neurodegenerative diseases including Alzheimer's disease (AD) and Lewy body diseases (LBD). In mild cognitive impairment (MCI) olfactory dysfunction heralds the progression to dementia. Olfactory dysfunction is associated with deposition of misfolded α-synuclein and hyperphosphorylated tau protein in the olfactory bulb (OB) and in other parts of the central olfactory system.
Methods: We examined 536 post mortem brains (mean age: 81.3 years, SE±0.46; 57 % male). Neuropathologically confirmed diagnoses were 33.6 % AD, 8.7 % LBD, i.e. Parkinson's disease with/without dementia, dementia with Lewy bodies, 5.4 % vascular dementia (VaD), 9.8 % other neurodegenerative diseases, and 42.3 % age matched controls. Sections of the OB were stained with antibodies against α-synuclein, tau and amyloid-β. The severity of the respective pathologies was assessed semiquantitatively.
Results: In the OB, tau, amyloid-β (Aβ) and α-synuclein correlated with neurofibrillary tangle Braak stages, Thal Aβ phases and Lewy body Braak stages, respectively. Mean scores were significantly higher in demented cases compared to controls ($P<0.01$). However, the correlation between OB α-synuclein pathology and clinical dementia failed to remain statistically significant when controlling for concomitant OB tau pathology: OB tau/amyloid-β was seen in 98.3 %/51.7 % of AD, and OB α-synuclein was present in 95.2 % of LBD. 85.7 %/23.8 % of LBD cases had OB tau/amyloid-β, while only 34.4 % of AD cases showed OB α-synuclein pathology.
Conclusions: Our data confirm that OB protein pathology is frequent in neurodegenerative diseases and accurately reflects the prevalence and severity of associated protein pathology in the brain. The high prevalence of OB tau in a considerable proportion of LBD patients warrants further studies to clarify whether olfactory dysfunction in LBD patients may be a biomarker for both cerebral α-synuclein and tau pathology, while OB tau pathology is a definite biomarker for progression of MCI to AD dementia.

A 15 Magnetization transfer ratio relates to cognitive impairment in normal elderly

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Objective: Magnetization transfer imaging (MTI) can detect microstructural brain tissue changes and thus may be a helpful adjunct in determining age-related cerebral damage. We investigated the association between the magnetization transfer ratio (MTR) in gray and white matter tissue compartments and cognitive functioning in a large community-based cohort over a wide age range.

Methods: We included 355 participants from the Austrian Stroke Prevention Family Study (ASPS-Fam) aged 38 to 86 years. MTR maps were generated for cortex, deep gray matter structures, white matter hyperintensities (WMH) and normal appearing white matter (NAWM). Comprehensive neuropsychological testing was done and we calculated composite measures for the domains of memory, executive function and motor skills. The associations between global and regional mean MTRs and domain-specific neuropsychological test performance were assessed by adjusted mixed models.

Results: The whole brain and lobar cortical MTR were directly and significantly related to performance on tests of memory, executive function and motor skills. There existed an almost linear dose-effect relationship. MTR of deep gray matter structures correlated with executive functioning and motor skills. All associations were independent of demographical factors, vascular risk factors, focal brain lesions and cortex volume.

Conclusions: Low MTR relates to cognitive impairment in middle aged and elderly individuals. The association is most pronounced for MTR changes in the cortex. Further research is needed to understand the basis of this association at the tissue level, and to determine the role of MTR in predicting cognitive decline and dementia.

A 16 R2* mapping for brain iron: associations with cognition in normal aging

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Objective: Brain iron accumulates during aging and has been associated with neurodegenerative disorders including Alzheimer´s disease. MR-based R2* mapping enables in vivo detection of iron content in brain tissue and thus may contribute defining at-risk groups for neurodegenerative diseases. We here investigated if during normal brain aging increasing iron load relates to cognitive impairment in region-specific patterns.

Methods: We included 355 participants from the Austrian Stroke Prevention Family

Study (ASPS-Fam) aged 38 to 86 years. All subjects were free of history or signs of neurologic disease. MR imaging and R2* mapping in the basal ganglia and neocortex was done at 3 T. Comprehensive neuropsychological testing assessed memory, executive function and psychomotor speed. The associations between R2*-based regional iron content and domain-specific neuropsychological test performance were assessed by adjusted mixed models. To test if iron effects on cognition were mediated by white matter lesion volume, brain infarcts or brain atrophy, we used simple mediation models for estimating indirect effect sizes.

Results: The highest R2*-determined iron concentration was seen in the globus pallidus. Pallidal iron was significantly and inversely associated with cognitive performance in all cognitive domains, except memory. The associations were dose-dependent. White matter hyperintensity volume, infarcts and brain atrophy did not mediate the relationship between iron and cognitive performance.

Interpretation: Higher R2* values in the globus pallidus, which can be attributed to increased iron deposition, correlate with cognitive impairment during brain aging independent of concomitant brain abnormalities. The prognostic significance of this finding needs to be determined.

A 17

Microstructural brain tissue damage in the hippocampus of AD patients: magnetization transfer imaging results from the prospective dementia registry in Austria (PRODEM)

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Objective: To localize areas of higher microstructural brain tissue damage in Alzheimer's disease (AD) patients compared to healthy controls (HC).

Methods: Our study cohort consisted of 48 PRODEM patients with probable AD (mean age 71 years, range 54–89; 52 % female; mean MMSE 21, range 12–28; mean disease duration 28 months, range 2–156), and 48 age- and sex matched HC. All subjects underwent 3 Tesla MRI including Magnetization Transfer Imaging (MTI). Voxel-based morphometry (VBM) was carried out to define areas of MTR differences between AD patients and HC. A general linear model (GLM) was built and adjusted for effects of atrophy via gray-matter density maps. For inference, we used the program Randomize. 5000 random permutations were performed to build the null distribution and a voxel-wise p-value<0.05, corrected for multiple comparisons, was considered statistically significant.

Results: Areas of higher microstructural tissue damage in AD than HC were found in the left hippocampus, left parietal- and occipital lobes, left insula and right frontal lobe. The changes were most prominent in the left hippocampus.

Conclusion: MTI detects microstructural brain tissue damage in patients with AD, independent of atrophy. The changes follow an AD-typical regional pattern. Whether groups of AD patients with identical severity of brain atrophy with presence or absence of additional MTR lowering show different rates of clinical progression or not, needs to be determined.

A 18 Anticardiolipin antibodies are associated with cognitive dysfunction in stroke-free individuals

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Background and purpose: The presence of anticardiolipin antibodies (aCLs) has been associated with vascular occlusive events. The role of aCLs as a risk factor for stroke has been a matter of debate, and scarce information exists on the relationship between aCLs and other cerebral disorders. Reports exist for seizures, chorea and subtle cognitive dysfunction. The association between aCLs and cognition was further explored and the relationship between aCL titres and brain magnetic resonance imaging (MRI) findings was evaluated in a large cohort of community-dwelling individuals.
Methods: The study cohort was drawn from the Austrian Stroke Prevention Study. A total of 1895 subjects had a complete risk factor assessment and measurement of aCL titres in serum. Participants were classified as aCL positive if either the immunoglobulin G (IgG) or IgM aCL titres were elevated (IgG>21 U/ml, IgM>12 U/ml). All subjects were also categorized based on the quartile distribution of IgG and IgM isotype titres. All underwent cognitive testing by the Mini Mental State Examination (MMSE) and a random sample of 947 participants also underwent brain MRI.
Results: aCL positive participants performed worse on the MMSE. IgG but not IgM isotype titres related to worse performance on the MMSE. No significant association existed with vascular brain abnormalities including lacunes, cortical infarcts and white matter lesions.
Conclusions: These data support the view that in normal elderly persons increasing IgG aCL titres relate to global cognitive dysfunction. It is unlikely that structural brain lesions are responsible for this finding.

A 19 Combining SPECT and EEG analysis for assessment of disorders with amnestic symptoms to enhance accuracy in early diagnostics

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Comparative evaluation of regional brain perfusion measured by single photon emission tomography (SPECT) and quantitative Electroencephalography (qEEG) analysis of persons with subjective cognitive complaints (SCC), with amnestic mild cognitive impairment (aMCI) and such with Alzheimer's disease (AD).
A total of 662 patients were investigated because of suspected cognitive dysfunction. After exclusion of patients with other forms of dementia than AD or relevant accompanying disorders, SPECT and qEEG data from 241 subjects (75 SCC, 100 aMCI, and 66 AD) were analyzed. Relative cerebral blood flow of 16 anatomical regions, relevant for neurodegenerative diseases, was assessed with automated analysis software (BRASS). Besides SPECT, each patient has also undergone EEG, which to date was neither statistically quantitatively evaluated (activity, complexity, mobility, brain rate, Hurst) on a group level, nor correlated with the SPECT results. Significant hypoperfusion measured with SPECT in areas relevant for neurodegenerative diseases in AD patients, is in accordance with recent publications.

Hypoperfusion could be demonstrated in four areas, which marginally miss significance for differentiating aMCI and SCC patients.
Quantitative analysis of EEG data shows significant differences between AD and SCC in many areas of the whole brain, especially brain rate and complexity are good markers in parietotemporal, central and post-temporal areas. Quantitative EEG data of aMCI and SCC patients in median/paramedian, parietotemporal and frontotemporal areas differ significantly as expected in neurodegenerative processes. Therefore, qEEG evaluation as an easy, cheap and non-invasive tool in routine use could serve for additional information in screening early cognitive dysfunction.

A 20

The peripheral sympathetic neuron is intact in Alzheimer's disease and frontotemporal dementia behavioural variant

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Introduction: 2012, Zakrzewska-Pniewska reported on a considerable high frequency (27 %) of Alzheimer's disease (AD) patients with pathologic sympathetic skin response test (SSR). The question arises whether the peripheral sympathetic sudomotor neuron might be involved in tauopathies frontotemporal dementia behavioural variant (bvFTD) and AD in analogy to involvement in alpha-synucleinopathies. A specific method to evaluate the postganglionic sympathetic sudomotor function is the Quantitative Sudomotor Axon Reflex Test (QSART). To our knowledge, this is the first prospective study to evaluate QSART in tauopathies.
Methods: Patients were recruited from the Department for Neurology, General Hospital, City of Linz. QSART was recorded from 4 standard recording sites (1 arm and 3 legs).
Results: 15 AD (7 female) and 14 bvFTD (9 female) patients were included. Mean age (+/-SD) of AD patients was 74+/-9, of bvFTD 71+/-10 years. Pathologic QSART was present in 3 (20 %) AD patients and 0 (0 %) of bvFTD patients (p=0.037). In the AD patients with pathologic QSART one had severe dysfunction and suffered concomitant diabetes mellitus; two minor dysfunctions of unknown origin. In no patient was the arm involved, the only site where sweating tested with QSART persists with increasing age. Sweat results of the 4 recording sites did not differ between the two groups.
Conclusion: There are no signs of sudomotor involvement in bvFTD in this exploratory study. Although a similar frequency of sudomotor involvement was observed in AD compared to Zakrzewska-Pniewska, our data suggests, that this finding is not part of the AD disease process but might rather be attributed to the high age.

A 21

D-cycloserine blocks human brain kynurenine aminotransferases

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Background: D-cycloserine, an antimycobacterial drug, since a few decades is known as a second-line drug for the treatment of tuberculosis and has been for a long time suggested as a partial agonist at the glycine site of the NMDA receptor. D-cycloserine exerts anticonvulsive properties in the chemically und electrically induced experimental epilepsy, shows improvement of cognition and exerts antidepressive effects. Clinical experiences revealed that D-cycloserine possible side effects are such as intoxication and/or epileptic manifestations.
Kynurenic acid, a well-known antagonist at the NMDA receptor with anticonvulsive properties is widely distributed in mammalian body and is significantly elevated in the brain of various neurologic and psychiatric disorders, and its involvement in the impairment of memory and cognition has been suggested. The aim of the study was to investigate the effect of D-cycloserine on kynurenic acid synthesizing enzymes in human brain, that is kynurenine aminotransferase I (KAT I), kynurenine aminotransferase II (KATII) and kynurenine aminotransferase III (KAT III).
Methods: Post-mortem human samples of frontal cortices of normal subjects (n=7) were from Institute of Neurology, Medical University Vienna. Enzymes activities of KATs were determined by measurement of synthesized kynurenic acid using HPLC method. One-way ANOVA analysis of variance and Student's T-test were applied.
Results: In post-mortem human brain homogenate D-cycloserine significantly and dose dependently (0.673; 6.73; 67.3 and 673 µM) lowered KAT I activity by 83.8; 76.4; 66.1 and 21.6 % of control, respectively, then KAT II by 82.3; 75.1; 53.2 and 6.8 % of control, respectively, and KAT III by 94.4; 80.9; 71.3 and 6.8 % of control, respectively. Higher D-cycloserine doses blocked KATs activities completely.
Discussion: For the first time our study demonstrates that D-cycloserine dose dependently is able to block human brain KAT I, KAT II and KAT III activities, in an in vitro study. Lowering of kynurenic acid due to D-cycloserine very likely is involved in the improvement of cognition and dementia, as reported. It needs to be clarified if the proposed effect of D-cycloserine as a partial NMDA receptor agonist is related to a direct drug action at the receptor or if the observed effect at the NMDA receptor is mainly due to lowered kynurenic acid content, as described.
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A 22

Vaskuläre Komorbidität bei Patienten mit frontotemporaler Demenz – Verhaltensvariante; Analyse klinischer, labormedizinischer und bildmorphologischer Parameter

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Die frontotemporale Demenz (FTD) ist eine degenerative Erkrankung, die vorwiegend den frontalen und temporalen Kortex betrifft. Die Klinik ist heterogen und der Befallsschwerpunkt variabel. Unter allen Demenzformen besteht eine Häufigkeit von ca. 5 %. Je nach führender Atrophie und vorherrschender Klinik unterscheiden sich drei Haupttypen: die frontotemporale Demenz Verhaltensvariante (FTDbv), die primär progressive nichtflüssige Aphasie und die semantische Demenz.

Über Komorbiditäten, insbesondere aus dem zerebrovaskulären Formenkreis, ist bis dato wenig bekannt.

In der vorliegenden Arbeit wurden zerebrovaskuläre Risikofaktoren (DM, Hypertonie, Hyperlipidämie, Serum-Homocystein, Nikotinabusus, Alkoholabusus) und Ereignisse (zerebrale Ischämien und Blutungen), entsprechende bildmorphologische Pathologien (zerebrale MRT) sowie duplexsonografische Befunde der extrakraniellen gehirnzuführenden Gefäße (Intima-Media-Dicke) und Medikamentenanamnese (Statine, Antihypertensiva, Antidiabetika) von Patienten mit der Diagnose einer FTDbv (n = 59) einer normalen Kontrollgruppe und Alzheimer-Patienten gegenübergestellt.

Die gewonnenen Ergebnisse werden berichtet.

Der interessante Fall

A 23 Progressive multifokale Leukenzephalopathie bei einem immunkompetenten Patienten – ein Fallbericht

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Hintergrund: Die progressive multifokale Leukenzephalopathie (PML) ist eine durch JC-Viren verursachte demyelinisierende ZNS-Erkrankung, zumeist bei zugrunde liegender Immunschwäche unterschiedlichster Ätiologie. Sehr selten tritt die PML bei Patienten ohne Immundefizit auf.

Fallbericht: Ein 65-jähriger Mann wurde aufgrund einer seit 18 Monaten bestehenden progredienten neurologischen Symptomatik aufgenommen. Anamnestisch wurden reduzierte kognitive Leistungsfähigkeit, Gangstörung, Schluckstörung und Sehstörungen angegeben. Bei Voruntersuchungen seien anfangs eine Demenzerkrankung, später ein atypisches Parkinson-Syndrom suspiziert worden.

Klinisch-neurologisch zeigten sich eine schwere Dysarthrie und Dysphagie, Hypomimie, Blickheberschwäche, massive Störung der Rumpfkontrolle mit Verlust der Geh- und Stehfähigkeit, eine zentrale Hemiparese links mit positiven Pyramidenbahnzeichen und eine links- und beinbetonte Ataxie.

Bereits in vorausgegangenen MRT des Cerebrums war eine supra- und infratentorielle Leukenzephalopathie, im Verlauf progredient, beschrieben. Trotz der fehlenden Anamnese für eine immunsupprimierende Erkrankung oder Therapie wurde aufgrund der Veränderungen in einer neuerlichen MRT an eine PML gedacht: Es bestanden offensichtlich mehrzeitige, beidseits in der weißen Substanz verteilte hyperintense Fokalläsionen mit Gewebsuntergang und Narbenbildung ohne die typischen Zeichen einer ischämischen Genese mit insgesamt rascher Progredienz. Die Diagnose wurde durch den PCR-Nachweis von JC-Viren im Liquor bestätigt.

Der Patient erhielt eine Therapie mit Mirtazapin, Mefloquin und Cidofovir. Acht Wochen nach Beginn der Therapie zeigte sich in der MRT erstmals ein stabiler Befund. Die klinisch-neurologischen Defizite waren jedoch progredient und der Patient verstarb vier Monate nach Diagnosestellung. Post mortem wurde die PML histologisch verifiziert. Ein Immundefizit oder eine maligne Grunderkrankung konnte trotz umfassender Durchuntersuchung, sowohl laborchemisch als auch bildgebend, nicht nachgewiesen werden.

Diskussion: Dieser Fall illustriert im Einklang mit publizierten Fallberichten, dass bei unklarer progredienter neurologischer Symptomatik mit progredienter Leukenzephalopathie im MRT auch bei nicht nachweisbarer Immunschwäche an das Vorliegen einer PML gedacht werden sollte.

A 24 Use PubMed and diagnose a rare disease in 10 minutes! Case report of a patient with adult onset Alexander's disease

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A 57-year-old, right-handed male was admitted to the intensive care unit for recurring asystolie, in need of a pacemaker implantation. After weaning, Parkinsonism and dysphagia came to attention. The neurological examination showed bradykinesia without tremor, tetra-ataxia, as well as dysarthric, bulbar speech. History revealed a chronic progressive course for 7 years. The patient's mother suffered from a gait disorder, which was never fully examined. Previous diagnostic work-up was inconclusive. A recent MRI of the brain showed symmetric white matter changes and a marked atrophy of medulla oblongata and spinal cord. Entering the following keywords in PubMed "atrophy medulla oblongata leukodystrophy" showed three publications, including one describing adult-onset Alexander's disease. In addition to characteristic but inconstantly present palatal myoclonus, lower brainstem and spinal cord atrophy are regarded as key features of the disease. Adult-onset Alexander's disease occurs due to a sense-mutation in the gene coding for the Glial Fibrillary Acidic Protein (GFAP). The detection of this mutation (c 1037 T>C het p L346S) proved the diagnosis in our patient.

A 25 Use of MRI, fMRI and DTI for interventional decision after minimal AVM haemorrhage

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A 48-year-old right-handed man was discovered with unruptured left occipital-parietal AVM at age 36. In 2011 he experienced a minimal haemorrhage at the anterolateral border of the AVM, causing no mass effect. His initial symptoms faded within 2 weeks. Decision on management was complicated by dominant hemisphere location, career function as teacher whose reading was from right-to-left word language function. Images demonstrated the precunial and high parietal AVM was fed from anterior, middle and posterior cerebral artery territories. fMRI demonstrated lexical function adjacent to parietal AVM border, possibly within the AVM. DTI showed visual pathways intact and displaced antero-lateral by the malformation. A growing number of fMRI references suggest lesion proximity to functionally important areas may produce misleading findings that functionally important tissues near the AVM are spared; high flow through the adjacent AVM may faile to show the small changes studied by fMRI. DTI reports include the AVM separate from or embedded in clinically-important pathways; the former predicted AVM removal may not be complicated by pathway disruption, the latter arguing it would. Ours is the first example where the pathway appears to be distorted/bent around the AVM, raising a new question whether the AVM has enlarged over time but has not directly involved an important pathway, and is it susceptible to safe removal as if it were subdural.
DTI may be more reliable in making management decisions compared to fMRI.
Intervention dilemma remains due to the difficulty of predicting the clinical outcome of lesion eradication.
Images are available for abstract presentation.

A 26

Multiple verkalkte intrazerebrale Metastasen eines invasiv duktalen Mammakarzinoms des Mannes: ein Fallbericht

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Mammakarzinome bei Männern sind selten und betragen nur etwa 1,6 % aller bösartigen Neubildungen der Brustdrüse. In etwa 16 % aller Mammakarzinome kommt es zum Auftreten intrazerebraler Metastasen. Wir berichten von einem 51-jährigen männlichen Patienten mit invasiv duktalem Mammakarzinom und multiplen kalzifizierten intrazerebralen Metastasen.

Nach modifiziert radikaler Mastektomie erfolgte eine adjuvante Chemotherapie mit Zyklophosphamid und Doxorubicin, antihormonelle Therapie und Gabe von Trastuzumab. Etwa ein Jahr nach Erstdiagnose kam es zum Auftreten eines erstmaligen generalisierten epileptischen Anfalls. Neuroradiologisch konnten multiple intrazerebrale kalzifizierte Läsionen nachgewiesen werden. Die histopathologische Aufbereitung ergab Metastasen des Mammakarzinoms. Daraufhin wurde eine palliative Ganzhirnbestrahlung mit insgesamt 30 Gy durchgeführt. Ein anschließendes Kontroll-Staging zeigte eine systemische Progression.

Kalzifizierte zerebrale Metastasen bei Mammakarzinomen sind in der Literatur sehr selten beschrieben. Die multiple Ausbreitung und die geringe bis fehlende Kontrastmittelaufnahme können differenzialdiagnostische Schwierigkeiten bereiten. Infektiologische Erkrankungen wie Tuberkulose, Toxoplasmose oder Zystizerkose sind hier in Erwägung zu ziehen.

Unklar bleibt, ob der Prozess der Kalzifikation charakteristisch für eine bestimmte Tumorbiologie ist, oder ob auch ein therapieassoziierter Effekt in Frage kommt.

A 27

Subacute spinal cord compression due to an intramedullar spinal teratoma in a 53-year-old female patient

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Benign intramedullary teratoma in adults causing spinal cord compression with painful subacute paraparesis are rare. This case study reports clinical and neuroradiological features as well as treatment and outcome. A 53-year-old woman complained about increasing lumbago over ten days. On admission, she had a bilateral L-4 radicular pain syndrome, more prominently to the right. The neurological examination showed no weakness of the lower extremities or any sensory deficits. Lasegue's sign was negative on both sides. The lumbar MRI showed an intraspinal intramedullar tumor at level T-11/T-12. From the radiological point of view, the tumor had a lipoma-like appearance, according to its homogenous tissue. Five days after admission a severe subacute progression of spinal signs and symptoms appeared. Clinical neurological examination revealed a sensorimotor transversal deficit at the level T-11 including a maximal deficit of the muscle strength of the left lower limb of 1/5 and the right lower limb of 3/5.

After onset of paraparesis, an intravenous dexamethason treatment was established

and an urgent neurosurgical intervention using intraoperative neurophysiological monitoring and ultrasound was performed. Histology revealed a mature intramedullar teratoma with mostly adipose tissue, and also parts of dermal tissue. Neurological examination ten days after surgery revealed almost normal muscle function.
This case of an intramedullar spinal teratoma in a 53-year-old female patient, presented clinically with a rapid progressive spinal cord compression. The radiological features of the lesion were mimicking a lipoma. Despite the fast progression of neurological signs and symptoms, the surgical decompression and cyst evacuation of the teratoma led to a good clinical outcome.

A 28

Pseudoneuritis vestibularis mit positionalem Downbeat-Nystagmus durch eine isolierte Läsion im Vestibulocerebellum

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Einleitung: Wir präsentieren den Fall eines 23-jährigen männlichen Patienten mit der Diagnose eines glioneuralen Tumors im Bereich des kaudalen Vermis. Postoperativ wies der Patient eine selektive Läsion von Nodulus und Uvula im unteren Vermis auf. Isolierte Läsionen in diesem Bereich ermöglichen Einblicke in die zentral-vestibuläre Funktion dieser vestibulozerebellaren Strukturen.
Methoden: Neben der klinisch-neurologischen Untersuchung wurde der Patient einer detaillierten vestibulären Diagnostik unterzogen. Die peripher- und zentral-vestibuläre Funktionsdiagnostik sowie die Okulomotoriktestung erfolgten mittels computergestützter Infrarot-Videookulografie (VOG) inklusive Rotationstests (System 2000, Micromedical Technologies Inc., Illinois, USA). Die Lagerungstests wurden mittels Videookulografie dokumentiert. Die Dokumentation der postoperativen selektiven vestibulozerebellaren Läsion erfolgte mittels MRT.
Ergebnisse: Postoperativ bestanden bei dem Patienten klinisch eine milde Gangunsicherheit und lageabhängige Vertigoepisoden. Im Head-Thrust-Test war der vestibulookuläre Reflex (VOR) seitengleich regelrecht ohne Korrektursakkaden auslösbar. In der MRT wurde eine isolierte Läsion des kaudalen Vermis (Nodulus und Uvula) diagnostiziert. In der Videookulografie wurde ein geringer torsioneller Spontannystagmus, jedoch kein Blickrichtungsnystagmus registriert. Sämtliche horizontalen und vertikalen Sakkadenparameter (Geschwindigkeit, Genauigkeit und Latenz) waren im Normbereich. „Smooth pursuit" war in allen Frequenzen mit normalem „gain" auslösbar (0,1 Hz: gain 0,91; 0,2 Hz: gain 0,83; 0,4 Hz: gain 0,87). Der VOR war in den Rotationstests symmetrisch mit disinhibiertem, hohem gain auslösbar (gain 0,9). Die Fixationssuppression des VOR während der Rotation war nahezu vollständig (gain 0,1). Bei Lagewechsel bzw. Re- oder Anteklination des Kopfes konnte ein reproduzierbarer positionaler Downbeat-Nystagmus mit langer Zeitkonstante und hoher Amplitude ausgelöst werden.
Diskussion: Diese seltene selektive Läsion des kaudalen Vermis des Patienten bestätigt die zentral-vestibuläre Funktion von Nodulus und Uvula. Insbesondere weist der hohe gain des VOR in den Rotationstests auf eine physiologisch inhibitorische Funktion dieser Strukturen auf den angulären VOR. Der positionale Downbeat-Nystagmus bestätigt zusätzlich die integrative Funktion von Nodulus und Uvula für Bogengangsafferenzen und dynamisch gravizeptive Otolithensignale aus Sacculus und Utriculus. In klinischer Hinsicht beweist der vorliegende Fall, dass isolierte vestibulozerebellare Läsionen peripher vestibuläre Störungen (im Sinne einer Pseudoneuritis vestibularis und eines Lagerungsnystagmus) simulieren können.

A 29 Dural arteriovenous fistula and concomitant cerebral sinus thrombosis – "The chicken or the egg?"

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Introduction: The relationship between dural arteriovenous fistulas (dAVF) and cerebral sinus thrombosis (CST) is complex and literature covering this topic is scarce.
Methods: Here we report a patient who developed CST with documented pre-existing dAVF.
Results: A 29 years old woman developed a pulsatile tinnitus in 2008 and work-up identified a type-I dAVF. Feeding arteries comprised branches from the left external carotid and vertebral arteries draining into the left sigmoid sinus. In 2008 and 2009 she underwent endovascular treatment with partial occlusion of the dAVF. In 2013 she presented to our emergency department with acute onset left-sided headache and was diagnosed with CST affecting superior sagittal, left transverse, left sigmoid sinus, and partially the right transverse sinus. She was treated with intravenous heparin followed by subcutaneous low molecular weight heparin (LMWH). Oral contraceptives were discontinued; no other risk factors for CST were identified. Headache markedly improved and the tinnitus resolved. A follow-up MRI showed nearly complete reperfusion of the cerebral sinuses. Catheter angiography after one month demonstrated spontaneous occlusion of the pre-existing vertebral artery fistula. A small middle meningeal artery-fistula was embolized. She continued receiving LMWH until now and further management will be decided after a follow-up MRI.
Conclusion: It is not uncommon to find that dAVF and CST develop together. So far, CST was mainly considered as the primary event that causes venous hypertension and subsequently the development of dAVF. However, the case reported here supports the hypothesis that dAVF may trigger the development of CST.

A 30 Diagnostische Herausforderung – Neuromyelitis optica

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Wir berichten über einen 64jährigen Patienten, bei dem klinisch und im Verlauf auch bildmorphologisch die Diagnose einer Neuromyelitis optica (NMO) gestellt werden konnte.
Anamnestisch relevant ist der Beginn der Erkrankung im Jahr 2010 mit einer leichten Gangstörung und Dysarthrie. In weiterer Folge erfolgten mehrfache Abklärungen im auswärtigen Krankenhaus mit Gangverschlechterung, Ataxie und einer beginnenden Paraparese der Beine in den Jahren 2012 und 2013.
Im April 2013 kam es zu einer klinischen Verschlechterung nach vorausgehendem Infekt ohne Fieber. Mit einer inkompletten sensiblen Querschnittssymptomatik ab TH 5 und einer leichten Paraparese der Beine wurde initial eine post-/parainfektiöse Genese der Myelitis postuliert und der Patient zu uns transferiert.
Die Liquor-Untersuchung ergab 13 Zellen/l bei sonst unauffälligem Befund und negativen Aquaporin-4-Antikörpern im Serum. Wiederholte Bildgebung der Wirbelsäule ergab keine sichere intramedulläre Läsion. Auch die zerebrale Bildgebung und die VEP waren unauffällig. Direkter Virus- sowie Antikörpernachweis für Borrelien, HSV, VZV, EBV, CMV, FSME, Adeno und Coxsackie-Virus im Blut und Liquor waren unauffällig. Unter einer Behandlung mit Kortison-Stoßtherapie (1 g Methylprednison mehrmals über je 5 Tage) und Azathioprin kam es jeweils nur zu einer kurzfristigen klinischen Besserung bei rekurrierenden schubförmigen klinischen Verschlechterungen bis zur passageren Paraplegie. Zu diesem Zeitpunkt im April 2013 wurden zwei Zyklen einer Plasmapherese an 5 konsekutiven Tagen eingesetzt. Unter dieser Therapie und mit intensiver physiotherapeutischer Behandlung konnte eine gute passagere Besserung der

Symptome erzielt werden. In der Bildgebung im August 2013 gelang der Nachweis langstreckiger signalhyperintenser Läsionen in der Medulla oblongata und im zervikalen Myelon mit Kontrastmittel-Enhancement. Zudem wurden symmetrische Läsionen im Mesencephalon, im Tectum, im Pedunculus cerebelli und entlang des Tractus corticospinalis beschrieben. Da es unter der Hochdosis-Azathioprin-Therapie zur weiteren klinischen Verschlechterung kam, wurde die Indikation für die Behandlung mit Rituximab gestellt und im Jänner 2014 begonnen.

Zusammenfassung: Die Diagnose NMO sollte unter Ausschluss der Differenzialdiagnosen klinisch gestellt werden, um aggressive und effektive Immunsuppressiva rechtzeitig einzusetzen. Bei initial negativer Bildgebung (spinal und zerebral) und negativen Aquaporin-4-Antikörpern ist die Diagnosestellung eine besondere Herausforderung.

A 31

Mitchondriale Erkrankung oder Autoimmunenzephalitis?

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Einleitung: Mitochondriale Erkrankungen können in jedem Lebensalter auftreten und manifestieren sich häufig durch neurologische Symptome wie epileptische Anfälle, Kopfschmerzen oder Muskelschwäche.

Fallbericht: Ein 52-jähriger, bislang gesunder Mann erleidet im Juni 2013 den ersten generalisierten tonisch-klonischen Krampfanfall. Postiktal kommt es zu einem prolongierten Psychosyndrom, die kognitive Leistung bleibt eingeschränkt im Sinne einer Akalkulie und einer sensorischen Aphasie. Das Schädel-MRT zeigt zunächst nur subkortikale Läsionen in occipitaler Betonung sowie eine Atrophie. Mittels Lumbalpunktion inkl. PCR kann eine Herpesenzephalitis ausgeschlossen werden. Der Nachweis von antineuronalen Antikörpern gelingt nicht.

Neben einer antiepileptischen Einstellung mit Levetiracetam erhält der Patient in dubio i. v. Immunglobuline wodurch es zu einer Verbesserung kommt, sodass er weitestgehend selbstständig wird.

Vier Monate später kommt es erneut zu einem tonisch-klonische Anfall, im Verlauf wird elektroenzephalografisch ein nichtkonvulsiver Status epilepticus der linken Hemisphäre festgestellt, welcher schließlich unter Levetiracetam, Lacosamid, Carbamazepin und Clobazam sistiert. Das Psychosyndrom verschlechtert sich zusehens. MR-tomografisch wird diesmal eine laminär-kortikale Hyperintensität links parieto-temporal prominent, vereinbar mit einem MELAS (mitochondriale Enzephalomyopathie, Lactatazidose und schlaganfallähnliche Episoden). Unterstützt wird die Verdachtsdiagnose einer mitochondrialen Erkrankung primär durch das muskelbioptische Vorliegen von *„red ragged fibres"* sowie Enzymveränderungen, während im Serum keine typischen Mutationen nachgewiesen werden können. Es erfolgt ein erneuter Therapieversuch mit Immunglobulinen i. v. sowie eine Prednison-Stoßtherapie, wodurch es einerseits zu einer deutlichen Verbesserung der Symptomatik, andererseits zu einer fast vollständigen Remission der kortikalen Hyperintensität links parieto-temporal kommt.

Diskussion: Die Muskelbiopsie und ein Schädel-MRT können mit einem MELAS (mitochondriale Enzephalomyopathie, Lactatazidose und schlaganfallähnliche Episoden) in Verbindung gebracht werden. Dahingegen lag weder eine Lactatazidose vor, noch konnten bis dato Mutationen an typischen Genompositionen identifiziert werden. Zum Zeitpunkt der Abstract-Verfassung ist das genetische Ergebnis einer erneuten Muskelbiopsie noch ausständig.

Das klinische Bild wäre mit einer Autoimmunenzephalitis vereinbar, der eventuell wegweisende Nachweis positiver Antikörper ist bislang noch nicht gelungen.

Schlüsselwörter: mitochondriale Erkrankung, *„red ragged fibres"*, Demenz, nichtkonvulsiver Status epilepticus.

A 32

GABA-B-Rezeptor-assoziierte limbische Enzephalitis mit Episoden von Hypoventilation und SUDEP

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Einleitung: Die GABA-B-Rezeptor-assoziierte limbische Enzephalitis ist eine seltene Erkrankung, die sich klinisch häufig mit Anfällen und Gedächtnisstörung manifestiert. Eine Assoziation mit einem kleinzelligen Bronchialkarzinom wird in über 50 % der Fälle beschrieben. Immuntherapie und/oder Malignombehandlung bei diagnostiziertem Tumor erbrachte in den meisten Fällen eine deutliche Verbesserung der neurologischen Symptomatik.
Fallbericht: Bei einem 65-jährigen Patienten trat erstmalig ein generalisierter tonisch-klonischer Anfall auf. Trotz eingeleiteter antiepileptischer Therapie traten bei unauffälligem MRT und EEG kurz darauf neuerliche GTKA und ausgeprägte Gedächtnisstörungen auf. Labordiagnostisch wurden im Serum GABA-B-Autoantikörper detektiert. Ein wiederholtes Tumor-Screening des Rauchers verlief negativ. Trotz antikonvulsiver und immunmodulatorischer Therapie mit Kortison, IVIG und Plasmapherese traten rezidivierend temporale und generalisierte Anfälle auf. Im Rahmen des dritten Zyklus der Plasmapherese kam es zu einem Atem- und Kreislaufstillstand mit sofortiger fünfminütiger kardiopulmonaler Reanimation. Nachfolgende MRT-Kontrollen wiesen keinerlei hypoxische Hirnschäden auf. In weiterer Folge kam es rezidivierend zu kurzen Phasen mit Tachykardie und spontan remittierender Hypoventilation und einer kontinuierlichen Vigilanzstörung. Durch Verabreichung von 2 Zyklen Rituximab konnten eine klinische Verbesserung der Vigilanz und eine Reduktion der Anfälle erreicht werden. Auf Grund des schlechten Allgemeinzustands konnte erst anschließend mit Zyklophosphamid begonnen werden. Hierdurch kam es zu einem Sistieren der Anfälle. Die antikonvulsive Therapie umfasste zuletzt eine Kombination aus Valproat, Levetiracetam und Lacosamid. Kurz vor Verabreichung des 3. Zyklus Zyklophosphamid kam es zu einer nächtlichen Asystolie, die kardiopulmonale Reanimation verlief erfolglos. Der neuropathologische Befund diagnostizierte SUDEP.
Diskussion: Bei fehlendem Hinweis auf ein Malignom kam es, trotz rascher Einleitung einer Immuntherapie mit Kortison, Immunglobulinen und Plasmapherese, zu einer Aggravierung der klinischen Symptomatik. Eine Therapie mit Rituximab und Zyklophosphamid erbrachte eine deutliche klinische Verbesserung mit Sistieren der Anfälle. Die aufgetretenen Episoden mit Hypoventilation deuten klinisch auf eine Hirnstammbeteiligung im Rahmen der Enzephalitis hin, wie es bisher nur bei z. B. NMDA-Ak-positiven limbischen Enzephalitiden beschrieben ist.

A 33

Multiple zerebrale Embolien bei VH-Flimmern – nicht kardiogen

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Fallbericht: Eine 78-jährige Patientin wurde mit apoplektiform aufgetretenem Schwindel und V. a. Schlaganfall stationär aufgenommen. Klinisch-neurologisch imponierten bei Aufnahme eine Dysarthrie, eine Fazialisparese links und ein Absinken im AVHV links (NIHSS 3). An Vorerkrankungen waren ein VHF (Therapie mit Marcoumar – INR 2,62), eine Kardiomyopathie, eine arterielle Hypertonie und ein Z. n. Arteriitis temporalis (Therapie mit Prednisolon) bekannt. Im initialen cMRT zeigten sich mehrfache punktför-

mige und kleinfleckige rezente Ischämien beidseits zerebellar und rechts parietal. Am Folgetag kam es zu einer akuten klinischen Verschlechterung (Somnolenz, Blickdeviation nach rechts, Plegie der linken oberen und hochgradige Parese der linken unteren Extremität – NIHSS 21). Im cMRT multiple, neu aufgetretene kleinfleckige Diffusionsstörungen (rechtshemisphärisch, zerebellar bds., im Stammganglienbereich und occipital links). In der durchgeführten kardialen Abklärung konnte das bekannte VHF bestätigt werden, es ergab sich jedoch kein Hinweis für kardiale Thromben. In der daraufhin durchgeführten weiteren Abklärung mittels CT-Angiografie zeigte sich ein Appositionsthrombus im proximalen Abschnitt des Truncus brachiocephalicus als mögliche Embolіequelle. Im Rahmen der therapeutischen Überlegungen wurden ein, durch die Neuroradiologie durchgeführtes Stenting (technisch mit neuroradiologischen Stents bei einem Durchmessers des Truncus brachiocephalicus von ca. 2 cm nicht möglich) sowie ein gefäßchirurgischer Eingriff (technisch möglich, aber bei vorbestehender Kardiomyopathie mit deutlich reduzierter EF nicht vertretbar) diskutiert. Schließlich wurde die Patientin in ein Zentrum mit der Möglichkeit der Implantation großlumiger Stents transferiert und es erfolgte die Therapie mit einem selbstexpandierenden Stent im Bereich des Truncus brachiocephalicus. Klinisch-neurologisch erholte sich die Patientin rasch (restitutio ad integrum).

Fazit: Obwohl es sich in diesem Fall um eine sehr seltene Schlaganfallätiologie handelt, sollte bei embolisch anmutenden Infarkten neben der kardialen Abklärung auch das supraaortale Gefäßsystem rasch untersucht werden!

A 34

Generalized reversible encephalopathy syndrome: a variant of posterior reversible encephalopathy syndrome (PRES)

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Posterior reversible encephalopathy syndrome (PRES) is a clinical-radiological syndrome, characterized by headache, visual disturbance, seizures and altered consciousness. Radiological findings show hyperintense T2-lesions on MRI, predominantly located in the subcortical white matter of the posterior occipital and parietal lobes.

We herein report the case of a 79-year-old female with adenocarcinoma of gastric cardia, which developed severe neurological signs and symptoms. MRI-imaging of the brain showed atypical generalized hyperintense lesions on T2 sequences.

Under symptomatic treatment, radiological changes as well neurological signs and symptoms improved. Several potential risk factors for PRES, such as hypertensive crisis, blood transfusions, infection and cancer were identified in our patient. Maybe the coexistence of these risk factors led to the unusual radiological and clinical manifestation of a generalized PRES variant.

A 35

Bing-Neel syndrome mimicking Lyme neuroborreliosis

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Purpose: Central nervous system (CNS) affection in Waldenstrom macroglobulinemia (WM) is called Bing-Neel Syndrome (BNS). We report it in a patient with peripheral paresis of the VII cranial nerve.

Case report: An 82-year-old man with ongoing WM was referred to our hospital due to intractable nocturnal pain in his legs.

Clinical manifestation was a mild hemiparesis on the right and a painful sensory and motor polyneuropathy of both legs. CCT detected a small old left middle cerebral artery infarction. Cerebrospinal fluid (CSF) showed 400 cells/µL. Penicillin G 20 Mega IE per day was given due to the assumption of CNS affection in Lyme disease (LD). Nocturnal pain improved but motor function of both legs worsened. Peripheral paresis of the VII cranial nerve on the right, impairment of cognition and urinary retention developed within days.

EMG displayed the active axonal demyelinization mostly of motor fibers and MRI confirmed affection of the equine cauda. CSF FACS analysis showed 98 % clonal CD 19+, CD20+ and CD79+ B-cells. CSF was negative for LD IgM, confirming BNS. The patient refused chemo or radiotherapy and died within two months.

Conclusion: Among the 35 BNS cases in English literature, impairment of cognition or vigilance, headache, body weakness and aphasia are frequent symptoms, however mimicking of neuroborreliosis was not reported before. Only FACS analysis of CSF confirmed the diagnosis of BNS in this case. Due to the pure prognosis of BNS, hematologists need to be alert to neurological symptoms in their patients.

Diagnostische Methoden

A 36 Normal aging of white matter measured by the bound pool fraction

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Introduction: While conventional MRI allows the assessment several macroscopic features of the ageing brain including the accumulation of white matter hyperintensities (WMH) and brain atrophy[1], microstructural changes remain largely undetected. The magnetization transfer (MT) ratio (MTR) has been proposed as a sensitive measure for assessing microstructural tissue changes[2, 3], but it is only a relative measure of the MT phenomenon. In this work, we therefore have hypothesized that the bound pool fraction (BPF) is more sensitive than the MTR for age related tissue changes such as extravascular widening, demyelination and tissue rarefication. The BPF is a fundamental parameter of the two-pool model[4] for brain tissue and reflects the macromolecular proton density involved in MT.

Subjects and Methods: The study cohort consisted of 99 healthy volunteers (39–80 years) with no history or signs of neuropsychiatric disorder. MRI was performed on a 3T Tim Trio and the BPF was mapped with a recently proposed sequence[5]. For comparison, a conventional MTR was obtained from a gradient echo sequence performed with and without an off-resonance saturation pulse. To assess MT in the WM regions we used the human brain WM atlas[6], registered nonlinearly to the MPRAGE scan from each volunteer using FSL FNIRT. A total of 29 regions were analyzed, where the left and right hemispheres were merged. The same procedure was applied on the MTR maps.

Results: BPF as well as MTR values showed a linear decrease with age in all WM regions. Although BPF maps had considerably more noise, they yielded a higher sensitivity for age related changes. The highest changes were found in the anterior corona radiata, followed by the posterior thalamic radiation.

Conclusion: While the MTR benefits from the high SNR of the underlying gradient echo sequence, this work proves that the BPF is more sensitive and therefore more specific for age related white matter changes. This is further supported by the observation that the age dependent decrease of the BPF is strongest in normal appearing areas where the highest density of age related WMH is usually expected. Further work will have to assess the relationship between local BPF changes, cognition and the prognostic values for the development of WMH.

1 Enzinger C et al., Neurology 2005
2 Ropele S et al., AJNR 2010
3 Rovaris M et al., Radiology 2003
4 Morrison C, Henkelman RM, MRM 1995
5 Soellinger M et al., MRM 2011
6 Oishi K et al., Neuro Image 2008

A 37

Zirkadianes Monitoring des funktionellen Handgebrauchs mittels bimanueller Aktigrafie in der Schlaganfallrehabilitation – eine Normdatenerhebung und erste klinische Fallbeispiele

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Hintergrund: Ziel der Studie war die zirkadiane Erhebung von Aktigrafie-Normdaten zum Rechts-links-Vergleich bei einer bestimmten funktionellen Tagesaktivität (Mittagessen), der Gesamtaktivität untertags sowie der Aktivität im Schlaf, um den klinischen Wert der Aktigrafie für die Schlaganfallrehabilitation bei Hemiparese zu beurteilen.

Methodik: 24 gesunde Probanden ohne Schlafstörungen aus dem medizinischem Personal unseres Zentrums erhielten für die Dauer von 24 Stunden jeweils einen Aktigrafen (SOMNOwatch™ – SOMNOmedics, Randersacker, Deutschland) am rechten und linken Handgelenk und protokollierten Dauer und Zeitpunkt der Mahl- und Bettzeiten sowie der Schlafqualität.

Ergebnisse: Bei 23 verwertbaren Aufzeichnungen (12 weiblich, 11 männlich, 19 Rechtshänder, 4 Linkshänder, Alter 39,1 ± 7,4 Jahre) war die Gesamtaktivität der dominanten Hand (42,9 ± 14,9 mg) im Vergleich zur nichtdominanten Hand (38,5 ± 11,8 mg) um 10 % höher (p = 0,001; range: –1 bis +25 %) und beim Mittagessen (dominant: 59,3 ± 18,8 mg vs. nichtdominant 48 ± 14,3 mg, p = 0,0001) um 19 % höher (range: –27 bis +54 %), während sich in der Nachtaktivität (rechts 5,9 ± 3,4 mg, links 5,9 ± 3,5 mg, p = ns) keine Unterschiede zeigten. Die Schlafeffizienz lag bei 93,1 ± 5,9 %. Ergänzend zeigen wir klinische Fallbeispiele aus Patientenmessungen.

Konklusion: Im zirkadianen Vergleich der dominanten mit der nichtdominanten Hand zeigen sich signifikante Unterschiede in der Gesamtaktivität und dem funktionellen Gebrauch der Arme beim Essen, jedoch keine Unterschiede in der Nachtaktivität. Die vorliegenden Patientenfälle zeigen eine objektive Änderung des funktionellen Handgebrauchs vor und nach Therapie.

A 38

The „own-name paradigm“ in functional diagnosis with fMRI in patients with severe chronic disorders of consciousness

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Background: In recent years, studies have shown that some patients with severe chronic disorders of consciousness may retain some residual higher brain functions. Thus, they may also preserve a certain level of consciousness, which however is difficult to detect in clinical bedside examinations. In this context, functional magnetic resonance imaging (fMRI) may represent a complementary method to the clinical assessment. Different paradigms are being tested on their suitability to detect residual consciousness.

The aim of this study is to examine if the "name paradigm" is an appropriate tool to distinguish between different stages of chronic disorders of consciousness – namely the Minimally Conscious State (MCS) and the Vegetative State (VS).

Subjects and methods: Using an event-related fMRI paradigm the brain activity of 19 VS patients and 7 MCS patients was measured during hearing a sentence containing the own first name or another unfamiliar first name (e.g. "Martin, hello Martin"). In the following, the resulting activations of the patients were compared to those of healthy controls in 7 regions of interest (ROI), which were determined in advance. At the beginning of the study all patients were clinically assessed in detail and diagnosed according to the Coma Recovery Scale-Revised and the Wessex Head Injury Matrix.

Result: 17 of 19 VS patients and 5 of 7 MCS patients showed similar activations as healthy controls. On average patients in a VS activated even more ROI than patients in a MCS. In each group two VS and MCS patients did not show any activation in the 7 ROI.

Conclusion: In the context of fMRI the name paradigm is not an appropriate diagnostic tool to distinguish between patients in a VS and those in a MCS. The results further allow two hypotheses: firstly, the own first name is at least partially processed automatically in the brain which is also possible in the absence of consciousness; secondly, contrary to the current definition of VS, these patients may still possess a residual language detection and self-consciousness.

A 39

MR-Diffusions-Tensor-Bildgebung und „fiber tracking" bei Rückenmarksläsionen

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Hintergrund: Die magnetresonanztomografische Diffusions-Tensor-Bildgebung (MR-DTI) ermöglicht die Visualisierung neuronaler Faserbündel innerhalb der weißen Substanz („Traktografie" oder „fiber tracking"). Während diese Methode beispielsweise in der präoperativen Planung bei raumfordernden intrakraniellen Tumoren regelmäßig angewandt wird, besteht mit intramedullären Läsionen nur wenig Erfahrung. Neuerungen erlauben mittlerweile technische Limitationen, Artefakte durch physiologische Ereignisse (wie zum Beispiel Atmung oder Herzschlag) und potenziell interagierende anatomische Strukturen besser zu umgehen und die Qualität deutlich zu verbessern.

Studienzweck: Es soll die klinische Anwendbarkeit zur Detektierung von Rückenmarksläsionen mittels MR-DTI in Zusammenschau mit dem klinisch-neurologischen Status und elektrophysiologischen Messungen untersucht werden.

Patienten und Methoden: Bei 10 Patienten (Alter 60,9 ± 21,3 a; 1 weiblich, 9 männlich) mit Rückenmarksläsionen (3 Patienten: A.-spinalis-anterior-Syndrom, 1 zervikal, 2 thorakal; 3 Patienten: kompressive Myelopathie, 3 zervikal, 1 thorakal; 2 Patienten: thorakale Myelitis, 1 Patient: psychogene Paraparese) wurde ein MR-DTI mit einem Philips-Achieva-3T-MRI-Scanner durchgeführt. Das Lähmungsausmaß wurde mittels ASIA-Skala klassifiziert (3 Patienten ASIA C, 6 Patienten ASIA D). Zusätzlich wurden bei jedem Patienten zeitnah elektrophysiologische Untersuchungen (somatosensorisch evozierte Potenziale und motorisch evozierte Potenziale) durchgeführt.

Resultate: Bei 8 Patienten konnte eine Rarefizierung beziehungsweise Diskonnektion der Fasern auf Läsionshöhe dargestellt werden, wobei die Beurteilbarkeit bei 1 Patienten durch auf ein Implantat zurückzuführende Suszeptibilitätsartefakte eingeschränkt war. Aufgrund von Bewegungsartefakten war die MR-DTI-Untersuchung bei einem Patienten nicht auswertbar. Keine Diskontinuität wurde bei dem Patienten mit der psychogenen Paraparese detektiert.

Konklusion: MR-„fiber tracking" ist in der Lage, Läsionen unterschiedlicher Ursache in verschiedenen Bereichen der weißen Substanz innerhalb des Rückenmarks zu erkennen. Die Quantifizierung des Läsionsausmaßes in Korrelation mit dem klinischen Erscheinungsbild und elektrophysiologischen Untersuchungen ist Teil gegenwärtiger Studien.

A 40 Neuritis of the lumbosacral plexus visualized by high-resolution sonography and MRI

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Background: Neuralgic amyotrophy of the lower extremity is a rare condition. We describe one case in which beside clinical and electrodiagnostic findings, high-resolution ultrasound (HRUS) and MRI could demonstrate the inflammatory process involving the lumbosacral plexus.
Case description: A 53-year-old male developed pain in the left hip with subacute onset over days, radiating towards the anterior thigh. Initial diagnosis of trochanteric bursitis led to local corticosteroid injection that brought like other NSAIDs – no pain relief. Consecutive neurological examination revealed discrete paresis of the left quadriceps. MRI of the lumbar spine showed no root compression. Electromyography of the anterior tibial muscle, the vastus lateralis and the iliopsoas muscle showed signs of neurogenic lesioning of the lumbosacral plexus or the roots L2 to L4. High-resolution ultrasound of the femoral nerve revealed extensive swelling of the femoral nerve. Its course was visible together with hypervascularisation and atrophy of the quadriceps femoris. Discrete signs of swelling were also detectable in the right femoral nerve. These findings were reproducible with MRI, where roots L2, L3 and L4 as well as the femoral nerve gave a hyperintense signal.
The patient was treated with corticosteroids and regained nearly full strength until last follow-up (four months after onset), while sonographic findings remained the same.
Conclusion: New imaging techniques are helpful additional tools for assessment of plexus neuritis and could be used as add-on to electrodiagnostics. Changes in ultrasound-appearance of peripheral nerves outlast duration of clinical symptoms after neuritis.

A 41 A concept to optimize gait rehabilitation in stroke patients during stationary and home rehabilitation using the wearable motion analysis system eSHOE

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Introduction: Gait deficits are very common in stroke survivors and affect up to 75 % of patients (Duncan et al., 2005). Only 5 % of patients gain independence in walking at discharge from a rehabilitation hospital (Paolucci et al., 2008). Deficits in walking can lead to impaired social life and falls which count as the most common medical complication after acute stroke. In modern neurorehabilitation, instrumented gait analyses are carried out to identify gait parameters and to evaluate the effectiveness of interventions. The MISTRAAL (Mobile Instrumented Stroke Rehabilitation in AAL) research project is an approach to increase rehabilitation output in both, in-patient and out-patient rehabilitation. The concept is based on monitoring and quantifying the progress of rehabilitation during the stationary rehabilitation and especially afterwards in the domestic area by extracting gait parameters from the eSHOE system.
Methods: eSHOE is a mobile motion analysis system consisting of a pair of orthopedic

insoles. Instrumented with a three-axis accelerometer, a three-axis gyroscope and force sensitive resistors, the system is capable of measuring kinematic and kinetic gait parameters. Automated algorithms using autocorrelation methods extract and calculate certain gait events and parameters. To provide feedback about the rehabilitation process to therapists and patients, a web-based platform will be developed to visualize the analyzed data and further patient-related information. Data transmission will be handled via a tablet PC and a mobile application that provides the interface between the tablet PC, platform and the central database.

For the examination of the suitability of the system architecture, a pilot study will be conducted at the neurological rehabilitation center NRZ Rosenhügel. Thirty patients involved will be using the eSHOE system during stationary rehabilitation and several selected will be using it after discharge rehabilitation at home.

Results: Preliminary results have shown that the eSHOE system in general, is applicable on motion data of pathological and physiological gaits. The developed feature extraction algorithms in combination with the data of two subject groups showed a high accuracy in detecting certain gait events. It has to be stated that the results are based on a geriatric population, hence they are not fully applicable on stroke patients.

Conclusion: Through this prior validation the eSHOE system is very likely to be a valid measurement system for monitoring and quantifying the progress of rehabilitation during the stationary rehabilitation and after discharge into the domestic area for rehabilitation at home.

Epilepsie

A 42 Consistency over time of electroencephalographic connectivity measures in temporal lobe epilepsy

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Connectivity biomarkers of the EEG have been shown to reflect seizure propagation and to indicate the source of abnormal hyperconnectivity. Nevertheless, it is questionable if these patterns are stable over time in different measures of connectivity. Moreover, it would be of interest whether the consistency over time differs between patients with epilepsy and healthy controls.

To address this topic we examined 9 healthy volunteers and 13 patients with temporal lobe epilepsy (TLE) on the right (5, mean age=36.8 years; SD=13.07; 3 women; one left-handed) and on the left (8, mean age=51.13 years; SD=10.13; 6 women; all right-handed). We calculated 14 measures of connectivity from two EEG-recordings separated by two weeks. We correlated these measures for each group and compared the correlations.

We found most consistent results for Granger-Geweke Causality. For this measure, consistency was found in a different network in healthy participants than in patients. Patients with a focus on the right side showed only a few consistent connections, mostly lateralized to the side of seizure onset, while patients with focus on the left side showed large bilateral consistencies, which were located frontocentrally over the left hemisphere and parietooccipitally over the right hemisphere.

The consistency of connectivity indicates that the pathological changes are a stable pattern in the EEG, being detectable for example with connectivity markers such as Granger-Geweke Causality. While the brain concert of information flow is generally variable, the high consistency, and thus, low variability on the focal region may reflect abnormal firing patterns. Additionally, the difference between left and right lateralized TLE could be a correlate of lateralization and TLE-induced reorganization of memory functions.

We demonstrated the necessity to ascertain the reliability over time of a particular connectivity-biomarker if used for pre-surgical analysis.

A 43 Emotion processing in patients with mesial temporal lobe epilepsy and amygdala lesions

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Background: Functional MRI (fMRI) studies have demonstrated a major role of amygdalae in processing of emotions. In mesial temporal lobe epilepsy (mTLE), amygdalae are often part of an epileptogenic zone. We aimed to test by fMRI how amygdala lesions are involved in an emotion response.
Methods: Twenty patients (9 women; median age 36 years, range 21–58) with mTLE due to unilateral lesions in amygdala and 19 healthy controls (10 women, median age 28 years, range 22–53) were tested with fMRI "dynamic fearful faces" paradigm: a short movie with alternating images of landscape and faces expressing fear. Median age at seizure onset was 24 years, range 6–50, and median epilepsy duration – 6 years, range 1–34. Seventeen patients (85 %) had drug resistant seizures; 18 (90 %) were right-handed. All patients underwent at least two high resolution MRIs (1.5 T) with an interval of at least six months for diagnostic purposes.
Results: fMRI signal in amygdalae was elicited in 55 % of patients and 74 % of healthy controls. Bilateral fMRI signal was observed more frequently in healthy controls compared to patients (53 % vs. 5 %, p=0.001). The majority of patients had left-sided mTLE (n=16, 80 %). In these patients, fMRI signal was seen equally ipsilateral and contralateral to epilepsy side (each 25 %); bilateral activation was rare (6 %). In right-sided mTLE patients (n=4, 20 %), only one had fMRI activation ipsilateral to epilepsy side; the rest (n=3) had no fMRI signal in amygdala.
Conclusions: fMRI activation patterns elicited by "dynamic fearful faces" paradigm differ between patients with unilateral mTLE and healthy controls. Integration of epileptogenic lesions of amygdalae into emotion processing might have important implications for possible post-surgical deficits in patients with drug resistant mTLE.

A 44 Experience with the new ILAE classification on focal cortical dysplasia in 60 patients

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Purpose: Up to 40 % of symptomatic childhood onset epilepsies are drug-resistant. About 50 % of them are due to malformations of cortical development (MCD). Resective epilepsy surgery has been increasingly performed in these patients, but reported outcomes have been variable and valid outcome predictors are currently not available.
Method: Included were all patients <18 years with drug-resistant epilepsies and histologically proven MCD, who had had epilepsy surgery at the Vienna pediatric epilepsy center and follow-up data of at least 12 months after surgery.
Clinical variables evaluated as possibly asso-

ciated with outcome after surgery were the following: gender, age at epilepsy onset, age at surgery, duration of epilepsy before surgery, preoperative febrile seizures, preoperative neurological deficits, type of seizure, lesion localization, preoperative seizure frequency, invasive recordings or type of MCD. Classification of MCD was according to the existing classification schemes of Barkovich et al., Palmini et al. and the novel ILAE classification of FCDs. Seizure outcome was classified using the ILAE proposal (Wieser et al.).

Results: We included 60 patients. One year after surgery 47/60 (78.3 %) patients were seizure-free (class 1a; ILAE). The result remained stable until the last follow-up visit (mean 4.4±3.2 years, minimal and maximal patient ages were one and 14 years, respectively). The decade-long follow-up showed that more than 50 % of the patients remained seizure-free following surgery (class 1a) at each annual control visit.
Extended lesion removal showed a statistically significantly better outcome than did tailored resections and partial disconnections (i.e. the best results were achieved with hemispherotomies). The type of MCD did not show significance.

Conclusion: We tried to evaluate the clinical applicability of the new ILAE classification system on Focal Cortical Dysplasia. However, in our patient group the extent of surgery remains the only predictor of seizure freedom.

A 45 *Language development after vertical perithalamic hemispherotomy*

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Purpose: To investigate language development after vertical perithalamic hemispherotomy and to determine possible prognostic factors.

Methods: Consecutive patients who underwent presurgical evaluation and functional hemispherotomy at the MUW Pediatric Epilepsy Surgery Program were identified from a prospectively maintained database. Inclusion criteria were regular follow-up visits at the centre including developmental data and a minimum follow-up period after surgery of 12 months. Developmental language quotients (DQ) before surgery and at the last follow-up visit were calculated for each child. In addition, associations between the postoperative DQ and the following possible prognostic factors were analyzed: age at epilepsy onset, duration of epilepsy, age at surgery, etiology, preoperative developmental status, postoperative seizure outcome, postoperative interictal EEG including sleep organization at 12 months after surgery. For statistical analysis, nonparametric Wilcoxon and Chi square tests were applied.

Results: Data from 30 children (15 female) were analyzed. The median follow-up duration after surgery was 4.0 years (+3.3 years). 28 patients (93.3 %) were seizure-free at 12 months and at the last follow-up visit. Thirteen patients (43.3 %) showed developmental progress at the last follow-up. Short duration of the disease, acquired pathology, lower preoperative DQ, persisting long-time seizure freedom, lack of epileptiform discharges in the contralateral (healthy) hemisphere after surgery, normal postoperative sleep patterns and the stopping of medication were predictive factors for a significant approach of the developmental age to the chronological age.

Conclusion: Vertical perithalamic hemispherotomy results in seizure freedom and developmental progress in a high percentage of children with early onset epileptic encephalopathies due to multilobar/hemispheric pathologies. Predictors of favorable language outcomes are short duration of the disease, acquired pathology, lower preoperative DQ, seizure freedom, lack of epileptiform discharges in the contralateral hemisphere after surgery, normal postoperative sleep patterns and the stopping of medication.

A 46 Is contralateral blink inhibition the cause of ictal ipsilateral eye blinking?

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Introduction: There is limited information on ictal unilateral eye blinking (UEB) as a lateralizing or localizing sign in focal seizures. We identified four patients with UEB and propose a novel mechanism of UEB based on a review of the literature.
Materials and methods: We report on four patients with intractable focal epilepsy showing UEB among 371 consecutive patients undergoing non-invasive video-EEG monitoring from October 2011 to December 2013.
Results: UEB was observed in 1.1 % (four of 371) of our patients. Two of them had right-sided TLE and two patients had FLE (one right and one left-sided).
Patient one had four right temporal seizures. Semiologic signs were impaired consciousness, bilateral eye blinking (BEB) and UEB on the right. During one seizure, BEB recurred after UEB with a higher blink frequency on the right. Ictal EEG onset was observed over F8 in 2/4, Fp2-F8 in 1/4 and Sp2-T2 in 1/4 seizures, respectively.
Patient two had ten left frontal seizures. Among them were one electrographic seizure and nine focal seizures with BEB (in 3/10) and one seizure with UEB on the left and ictal EEG onset over F7.
Patient three had six right frontal seizures arising from sleep (in 6/6) with hypermotoric symptomatic (in 6/6 seizures, respectively). UEB right was observed in 1/6 seizures with ictal EEG onset over F4.
Patient four had three right temporal seizures, arising from sleep (in 2/3), showing oroalimentary automatisms (in 3/3), dystonic posturing of the right arm (in 1/3), tonic posturing of the left hand (in 1/3) and postictal nose-whipping right (in 1/3 seizures, respectively). UEB right was observed in 2/3 seizures with ictal EEG onset over T2.
None of the patients displayed any clonic activity of the face.
Discussion: UEB was observed in patients with FLE and TLE. UEB was ipsilateral to the ictal EEG pattern in all patients. The asymmetric blink frequency during BEB in patient one leads to the hypothesis that ictal UEB is caused by contralateral blink inhibition, due to activation in frontotemporal cortical areas and mediated by trigeminal fibres.

A 47 Emotion, affect and prosody recognition in patients with mesial temporal lobe epilepsy and amygdala lesions

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Background: The amygdalae are considered to be a constitutive element in the processing of emotions. In patients with mesial temporal lobe epilepsy (mTLE), the amygdalae are often part of the epileptogenic zone. We aimed to identify a possible association between fMRI activation of the amygdalae and facial emotion affect as well as prosody recognition in patients with mTLE and amygdala lesions.
Methods: Seventeen patients (8 women; median age 36 years, range 21–58) with

mTLE due to unilateral probable dysplastic amygdala (pDA; right-sided 4, left-sided 13) were tested with the "fearful face" fMRI paradigm using video sequences with alternating images of faces expressing fear and landscapes. Furthermore, the Comprehensive Affect Testing System (CATS) was used to measure emotion, affect and prosody recognition. Median age at seizure onset was 24 years (range 6–50), the median epilepsy duration was 6 years (range 1–34). Amygdala lesions were identified on high resolution MRI (1.5 T).

Results: In 7/17 (41 %) patients, a unilateral activation (right-sided 4, left-sided 3) of the amygdalae was observed. 6 (86 %) out of these patients showed deficits in prosody recognition, 3 (43 %) in emotion recognition and one (14 %) in affect recognition. In 9/17 (53 %) patients, no fMRI activation of the amygdalae but only a few impairments concerning prosody recognition (n=2, 22 %) and emotion recognition (n=1, 11 %) were seen. In one patient (6 %), a bilateral fMRI signal as well as average CATS scores was elicited.

Conclusions: Emotion and affect recognition is intact in the majority of patients with unilateral pDA and mTLE. Prosody recognition is most likely to be impaired. Furthermore, these data show no strong association between absent activations of the amygdalae in fMRI and deficits in emotion processing as depicted in the Comprehensive Affect Testing System (CATS) quotient scales.

A 48 *Ventral occipitotemporal high-gamma activity recorded with ECoG during a numeric counting task*

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Introduction: Event-related responses in the high-gamma frequency range (>60 Hz) have been observed in many different functional brain systems. For example, a recent study used intracranial EEG and showed significant activation in the inferior temporal gyrus in the frequency range between 60–170 Hz in response to visually presented numerals[1]. Other, fMRI based studies, revealed the involvement of the occipitotemporal region in abacus-based mental calculation tasks[2, 3]. In the present work, we want to demonstrate the involvement of the ventral occipitotemporal region in an abacus-based counting/arithmetic task using functional ECoG mapping.

Methods: Data were collected with a 256-channel g.HIamp system (g.tec, Austria) connected to the cortiQ system for real-time functional mapping (g.tec, Austria). cortiQ presented the stimuli and acquired and stored the data. Data were collected from a right-handed female patient with epilepsy who had 236 subdural electrodes implanted. These electrodes covered the left frontal-, left temporal- and left parietal/occipital lobe, the right temporal lobe, as well as the left and right temporal base. The subject performed three runs of a counting task and was asked to count from a given number (e.g., 300) either upwards or downwards in fixed steps during the recording procedure.

Results: Our analyses indicated significant task-related activations in the right ventral occipitotemporal region. These activations were consistent across all three recorded data sets. We also noted smaller effects in different electrodes over the temporal lobe.

Conclusion: In our ongoing study, we identified locations in the occipitotemporal region that responded to an abacus-based counting task by using functional ECoG data. As the cortiQ system can highlight such task-related areas directly at the bedside, and because its operation does not depend on experts in signal processing, it should be useful for mapping function in areas that cannot readily be mapped using electrical stimulation mapping (i.e., areas other than primary motor/sensory/language areas).

1 Shum J et al., A Brain Area for Visual Numerals. J Neurosci 17 April 2013; 33(16):6709–715

2 Du F et al., Abacus Training Modulates the Neural Correlates of Exact and Approximate Calculations in Chinese Children: An fMRI Study. BioMed Res Int 2013; Article ID 694075

3 Li Y et al., Structural changes in left fusiform areas and associated fiber connections in children with abacus training: evidence from morphometry and tractography. Front Hum Neurosci 2013; 7:335

A 49

Status epilepticus: Severity Score oder epidemiologiebasierter Mortalitäts-Score? Ein retrospektiver explorativer Vergleich

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Hintergrund: Der Status epilepticus (SE) stellt einen neurologischen Notfall mit hoher Mortalität dar. Bislang stand nur der „SE Severity Score" (STESS) zur individuellen Prognoseabschätzung zur Verfügung. Wir entwickelten den flexiblen epidemiologiebasierten Mortalitäts-Score für SE (EMSE), der aus einer Kombination der Domänen Ätiologie (E), Alter (A), Komorbidität (M), Dauer (D), EEG (D) und Bewusstseinslage (C) zusammengesetzt ist, und verglichen ihn bezüglich der diagnostischen Aussagekraft mit STESS.
Methoden: 112 konsekutive SE-Episoden bei 92 nichthypoxischen und 11 hypoxischen Patienten an einer neurologischen Intensivstation einer Universitätsklinik (Tertiärversorgung) wurden retrospektiv untersucht. Die Punkteanzahl für die verschiedenen Domänen wurde rezenten Publikationen in Form spezifischer Mortalitätsraten entnommen. Grenzwerte der Summen-Scores wurden für jede Kombination der Domänen vom niedrigsten Wert der Verstorbenen abgeleitet (explorativer Zugang). Sensititvität, Spezifität, negativer (NPV) und positiver prädiktiver Wert (PPV) sowie Anzahl korrekt Klassifizierter von EMSE wurden mit STESS mit zwei verschiedenen Grenzwerten (STESS-3, STESS-4) verglichen.
Ergebnisse: EMSE mit der Kombination Ätiologie-Alter-Komorbidität-EEG (EAMN) war STESS-3 und STESS-4 überlegen (NPV 100 %, PPV 68,8 %, korrekt Klassifizierte 89,1 %, $p = 0{,}0022$ oder niedriger, Signifikanz des p-Wertes nach Korrektur für multiples Testen $p \leq 0{,}0044$).
Schlussfolgerungen: Der EMSE-Score EAMN erklärte die Mortalität in etwa 90 % der Patienten und war STESS signifikant überlegen. Diese explorative Studie muss extern prospektiv evaluiert werden. EMSE kann an verschiedene Regionen und über die Zeit dem medizinischen Fortschritt angepasst werden. EMSE kann sich als wertvolles Instrument zur Risikostratifizierung bei Interventionsstudien erweisen. Komorbidität spielte eine wichtige Rolle für die Outcome-Abschätzung in dieser Studie.

A 50 Therapieansprechen und Nebenwirkungen einer Zusatztherapie mit Perampanel

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Hintergrund: Perampanel (PER) ist ein nicht kompetitiver AMPA-Rezeptor-Antagonist, der seit Juli 2012 zur Zusatztherapie bei fokalen Epilepsiesyndromen bei Erwachsenen zugelassen ist.
Methoden: Prospektive Erfassung von Therapieansprechen und Nebenwirkungen einer Zusatztherapie mit PER bei 70 Patienten mit fokaler Epilepsie zwischen 09/2012 und 11/2013.
Resultate: Siebzig Patienten (61 % weiblich) mit fokalen Epilepsiesyndromen erhielten eine Zusatztherapie mit PER seit 09/2012. Das durchschnittliche Alter zu Therapiebeginn lag bei 41,7 Jahren (Standardabweichung [SD] 18,9), das durchschnittliche Follow-up betrug 8,2 Monate (SD 3,3). Vierundsechzig Patienten nahmen PER zum Zeitpunkt des letzten Follow-ups (13. 11. 2013) länger als drei Monate ein. Sechsundvierzig Patienten (66 %) waren zum Zeitpunkt des letzten Follow-ups weiterhin unter Therapie mit PER, wovon sechs Patienten (6/46; 13 %) anfallsfrei waren, sechs Patienten (6/46; 13 %) eine Reduktion der Anfallsfrequenz über 50 % und 20 Patienten (20/46; 39 %) keine Abnahme der Anfallsfrequenz berichteten. Die durchschnittliche Anfallsfrequenz vor Therapiebeginn mit PER betrug 8,1 Anfälle/Monat (SD 14,6), die durchschnittliche Anfallsfrequenz zum Zeitpunkt des letzten Follow-ups lag bei 5,0 Anfällen/Monat (SD 8,0). Fünfunddreißig Patienten (35/70; 50 %) berichteten über Nebenwirkungen unter Therapie mit PER, wobei Schwindel (23/70; 33 %) und Abgeschlagenheit (8/70; 11 %) die häufigsten Nebenwirkungen waren, gefolgt von Übelkeit (4/70; 6 %), Konzentrationsstörungen (5/70; 7 %) und psychiatrischen Nebenwirkungen (6/70; 9 %). Bei 11 Patienten (15 %) erfolgte aufgrund von Nebenwirkungen eine Dosisreduktion mit nachfolgender Besserung, bei 19 Patienten (27 %) wurde PER aufgrund der Nebenwirkungen abgesetzt. Neunundzwanzig Patienten (41 %) nahmen zeitgleich zur Therapie mit PER einen Enzyminduktor ein, wobei sich kein Unterschied in der Dosierung (p = 0,249), dem Auftreten von Nebenwirkungen (p = 0,283) oder dem Therapieansprechen (p = 0,263) zeigte.
Schlussfolgerung: PER ist gut wirksam in der Zusatztherapie fokaler Epilepsiesyndrome und führt zu einer Reduktion der Anfallsfrequenz > 50 % bei 26 % der Patienten. Nebenwirkungen, insbesondere Schwindel, sind häufig (50 %), können jedoch durch Dosisreduktion und Einnahme kurz vor dem Zubettgehen reduziert werden. Tolerabilität und Therapieansprechen unterscheiden sich nicht bei zeitgleicher Einnahme eines Enzyminduktors.

A 51 Intravenöse Ketamintherapie bei refraktärem Status epilepticus

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Einleitung: Der therapierefraktäre Status epilepticus (RSE) stellt eine therapeutische Herausforderung dar und ist definiert als Status epilepticus (SE), welcher trotz Applikation von Benzodiazepinen und Antiepileptika (AED) in adäquater Dosierung nicht durchbrochen werden kann. Ketamin ist ein nichtkompetitiver NMDA-Rezeptor-Antagonist. Über die Anwendung in RSE berichten einige Fallberichte und retrospektive Serien. Ziel der Studie ist, die Verträglichkeit und Wirkung hinsichtlich Ketamin in RSE darzustellen.
Methoden: Monozentrische, retrospektive Studie; die Daten aller zwischen 2011 und 2013 auf der neurologischen Intensivstation wegen eines SE behandelten Patienten (n = 219) wurden analysiert; Dosierung, Wirkung, mögliche Nebenwirkungen von Ketamin, Ätiologie, Dauer, Typ des SE sowie Zusatzmedikation wurden erhoben.
Ergebnisse: In 26/219 Patienten (medianes Alter zum Zeitpunkt des SE 64,5 Jahre, SPW 15–80) wurde Ketamin in Form von Ketamin S in Kombination mit Midazolam verabreicht. Alle Patienten wiesen ein initial fehlendes Ansprechen auf Benzodiazepine und Standard-AED auf.

Ursachen für RSE: 8/26 Patienten Hypoxie, 4/26 systemische Infektionen, 4/26 ischämische/hämorrhagische Schlaganfälle, 6/26 unklar, 4/26 vorbestehende Epilepsie
Typen von RSE: 2/26 myoklonischer SE, 5/26 konvulsiver SE (CSE), 15/26 nonkonvulsiver SE (NCSE), 3/26 CSE mit Übergang in NCSE, 1/26 fokaler SE übergehend in NCSE
Anwendung von Ketamin: Beginn median 3,5 Tage (SPW 1–20) nach Beginn des SE; mediane Dauer der Ketamintherapie 5 Tage (SPW 1–16) bzw. 96 Stunden (SPW 8–355); mediane Dosis betrug 1,91 mg/kg/h (SPW 0,11–4,68) bzw. 150 mg/h (SPW 12,5–375).
Bei 6/26 Patienten wurde die Therapie mit einem Bolus (median 200 mg, SPW 200–300), bei 20 Patienten mit einer kontinuierlichen Infusion (median 200 mg/h, SPW 50–375) begonnen. In 12/26 Patienten wurde Ketamin als letztes Medikament appliziert und der RSE durchbrochen; 14/26 Patienten starben an RSE, Grunderkrankung oder deren Folgen.
Schlussfolgerung: Ketamin kann im späten Stadium des RSE nach Versagen von Benzodiazepinen und AED als effiziente Therapie eingesetzt werden. Allerdings besteht angesichts des RSE und der Grunderkrankungen eine hohe Mortalität.

A 52

Reduced kynurenic acid in canine epilepsy

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Background: Kynurenic acid, a tryptophan metabolite, is a well-known endogenous antagonist of the glutamate ionotropic excitatory amino acid receptors and of the nicotine cholinergic subtype 7α receptor and its neuroprotective and anticonvulsive activities has been demonstrated in various animal models of neurodegenerative diseases. Beside that there are data suggesting involvement of kynurenic acid in various dementia processes. Alterations of kynurenic acid levels have been reported in experimental mammalian epilepsy and human epilepsy. In this study we investigated tryptophan and kynurenic acid levels in cerebrospinal fluid and serum of epileptic dogs.

Methods: Cerebrospinal fluid and serum of epileptic dogs (n=14) and of control subjects (n=19) were used. Study was performed according to Austrian ethical regulations. Determination of tryptophan and kynurenic acid concentration was performed using a high performance liquid chromatography method. One-way ANOVA analysis of variance and Student's T-test were applied.

Results: A significant reduction of tryptophan content (ca. 25 % of control; $p<0.05$) was found in the cerebrospinal fluid of dogs with idiopathic and symptomatic epilepsy. No alteration of tryptophan levels was found in the serum of epileptic dogs, when compared to controls. A significant reduction of kynurenic acid level was observed in the cerebrospinal fluid of dogs with idiopathic epilepsy (48 % of control; $p<0.01$). In dogs with symptomatic epilepsy the reduction of kynurenic acid in cerebrospinal fluid was only moderately and not significantly altered. Kynurenic acid in the serum was moderately and not significantly reduced.

Discussion: Obtained data revealed changes of tryptophan metabolism in cerebrospinal fluid in canine epilepsy. Lowering of tryptophan levels in epileptic dogs would suggest increased tryptophan metabolism along kynurenine pathway in the CNS and formation of convulsive and neurotoxic metabolite quinolinic acid. Lowered kynurenic acid in the CNS could be in part responsible for the seizures activities.

Freie Themen

A 53 Genome-wide association study of white matter lesion progression

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Objective: White matter lesion (WML) progression is related to cognitive decline and stroke, but its determinants besides baseline WML load are largely unknown. Here we tested the hypothesis that WML progression is highly heritable and that common genetic variants explain a considerable proportion of the variance of WML progression in an elderly population can be identified.

Methods: We included 5991 elderly individuals without stroke or dementia from 9 community-based cohorts in the present investigation. WML progression was rated as present or absent based on validated visual rating scales or semiquantitative measurement of WML volume change. Heritability of WML progression was calculated based on family structure in the Framingham Heart Study. A genome-wide association study using logistic regression adjusted for age, sex, follow-up time and baseline WML load was performed in each cohort. Fixed effect meta-analyses were performed to estimate effect size and standard errors.

The relative contribution of genetic factors in explaining the variance in progression of WML was assessed by comparison of risk models including demographics and vascular risk factors versus models including the clinical information plus all SNPs that have been shown to be associated with WML occurrence in current and previous studies.

Results: A total of 925 (15.9 %) subjects showed WML progression. The family-based heritability estimate for WML progression was low at 6.5 %. In the adjusted meta-analysis no SNPs achieved genome wide significance (p-value <5 x 10–8). Three loci were suggestive (p-value <5 x 10–5) on chromosomes: 8q22.1 containing genes encoding RUNX1T1; 12q13.13, SLC4A8; and 16q22.3, PMFBP1.

These SNPs and genetic variants that have been related to WML burden in previous investigations explained only 7.7 % more of the variance of WML progression than age, vascular risk factors and baseline WML volume alone.

Interpretation: Genetic factors contribute little to the propagation of age-related WML. Future research on modifiers of WML progression needs to focus on non-genetic environmental and life-style-related factors.

A 54

RAGE (receptor for advanced glycation endproducts) and the RAGE ligand HMGB1 (high mobility group box-1) and their role in thymic epithelial tumors and regular thymic morphology

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Objective: Recently, a role of the Receptor for Advanced Glycation Endproducts (RAGE) in Myasthenia gravis (MG) was described. We herein investigated the role of RAGE and one of its ligands (HMGB1) in Thymic Epithelial Tumors (TETs), Thymic Hyperplasia (TH) and Regular Thymic Morphology.

Methods: To verify whether these molecules are involved in thymic pathologies we applied immunohistochemical analyses in 33 cases of TETs and 21 non-neoplastic thymuses. These results were corroborated by systemic measurements (ELISAs) of serum in 41 patients with TETs, 28 patients with TH and 48 volunteers.

Results: RAGE and HMGB1 are both expressed in TETs as well as in regular thymic morphology. We have observed the strongest cytoplasmic RAGE expression in WHO type B2 thymomas and thymic carcinomas ($p<0.001$). The nuclear HMGB1 staining was strongest in A and AB thymomas; conversely the cytoplasmic staining was strongest in B1 thymomas ($p<0.001$). In serum the levels of soluble RAGE (sRAGE) were significantly reduced in TETs ($p=0.008$) and in invasive tumor stages ($p=0.008$), whereas the levels of HMGB1 were significantly increased ($p=0.008$).

Fetal thymuses showed a strong RAGE expression of subcapsular epithelial cells, which was also found in 50 % of myasthenic patients. Further, RAGE was specifically expressed in Hassall's corpuscles, macrophages, thymic medulla and in germinal center cells of patients with follicular hyperplasia.

Conclusion: Thus, RAGE and HMGB1 are involved in thymic malignancies as well as in regular thymic morphology. The different thymic and systemic expression of these molecules may act as diagnostic or therapeutic targets in cancer and autoimmunity.

A 55

Klinische Epidemiologie des benignen paroxysmalen Lagerungsschwindels: eine retrospektive Studie aus einem tertiären Zentrum

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Einleitung: Der benigne paroxysmale Lagerungsschwindel (BPPV) stellt die häufigste Ursache von Schwindelbeschwerden in der klinischen Praxis dar. Die einfachen diagnostischen und therapeutischen Manöver ermöglichen eine rasche Abklärung und Therapie der Symptome. In der vorliegenden Studie wurden klinisch-epidemiologische Daten von Patienten mit diagnostiziertem BPPV erhoben, um mögliche kausalgenetische Faktoren des BPPV weiter abzugrenzen.
Methoden: Wir erfassten retrospektiv die Daten von 296 konsekutiven Patienten mit der gesicherten Diagnose eines BPPV, die im Zeitraum von 2007 bis 2010 an der Medizinischen Universität Wien aufgrund von Schwindelsymptomen neurologisch begutachtet wurden. Die Datenanalyse umfasste sowohl Patienten aus der Notfallaufnahme, der neurologischen Akutambulanz, der Spezialambulanz für Gleichgewichtsstörungen und den neurologischen Stationen.
Ergebnisse: Insgesamt wurden 296 Patienten mit klinisch gesichertem BPPV erfasst. Das Alter der Patienten betrug im Durchschnitt 60,8 Jahre (± 15,7 Jahre, Alters-Range: 25–99 Jahre). Von den Betroffenen waren 70,1 % weiblich und 29,9 % männlich (f/m-Ratio: 2,34/1). Die häufigste Form des BPPV war jene des posterioren Bogenganges (90 %), gefolgt von jener des horizontalen (7 %) und der des anterioren Bogenganges (2 %). Bei 1 % der Patienten war der betroffene Bogengang retrospektiv nicht bestimmbar. Die rechte bzw. die linke Seite waren bei allen Bogengängen nahezu gleich häufig betroffen (rechts 44 %, links 42 %). Bei 9 % der Patienten war eine bilaterale Symptomatik auslösbar, während bei 5 % der Patienten die Seitenlokalisation retrospektiv nicht möglich war. Die Mehrzahl der Patienten (82,1 %) konnten bereits mit einer einmaligen bzw. max. zweimaligen Behandlung therapiert werden, bei 17,9 % waren mehrere Therapiekontrollen erforderlich. Die therapierefraktären Fälle waren überwiegend jene mit Affektion des posterioren Bogenganges (92 %), gefolgt von jenen des horizontalen (6 %) und des anterioren (2 %) Bogenganges. In den untersuchten 4 Jahren trat die BPPV-Symptomatik der Patienten in 54 % der Fälle in den kalten und in 46 % in den warmen Jahreszeiten auf.
Diskussion: Die erhobenen Daten bestätigen, dass der BPPV vorwiegend eine Erkrankung des höheren Lebensalters darstellt, jedoch einen großen Alters-Range aufweist. Frauen sind mehr als doppelt so häufig betroffen wie Männer. Die überwiegende Form des BPPV ist jene des posterioren Bogenganges, gefolgt von jener des horizontalen und des anterioren Bogenganges. Ferner konnte gezeigt werden, dass beide Seiten nahezu gleich häufig betroffen sind und fast 10 % der Patienten bilaterale Symptome aufweisen. Die Symptomremission gelingt nach 1–2-maliger Behandlung in über 80 % der Fälle.
Die vorliegenden Ergebnisse werden mit bisherigen epidemiologischen Daten verglichen und mögliche kausalgenetische Faktoren des BPPV diskutiert.

A 56 Aging-associated changes in the motor control of ankle movements in the brain

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Although age-related gait changes have been well characterized, little is known regarding potential functional changes in central motor control of distal lower limb movements with age. We hypothesised that there are age-related changes in brain activity associated with the control of repetitive ankle movements, an element of gait feasible for study with functional magnetic resonance imaging (fMRI). We analyzed standardized fMRI data from 102 right-foot dominant healthy subjects aged 20–83 years for age-associated effects using FSL and a meta-analysis employing coordinate-based activation likelihood estimation (ALE). For the first time, we have confirmed age-related changes in brain activity with this gait related movement of the lower limb in a large population. Increasing age correlated strongly with increased movement-associated activity in the cerebellum and precuneus. Given that task performance did not vary with age, we interpret these changes as potentially compensatory for other age-related changes in the sensorimotor network responsible for control of limb function.

A 57 The superficial branch of the radial nerve – US-guided perineural infiltration with anatomical correlation

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This cadaver study's aim is to evaluate the feasibility of an ultrasound guided perineural infiltration of the different segments of the superficial branch of the radial nerve (SBRN) as a potential therapeutic option in Wartenberg's syndrome.
21 arms from 11 non-embalmed cadavers were examined with ultrasound (US). Under US guidance a perineural injection with ink was performed proximal to the site, where the SBRN perforates the forearm fascia. In the following dissection we evaluated the ink's distribution around the nerve.
US allowed the distinction of the SBRN's different segments and their relation to the fascia. In all cases the subfascial segment was stained. In one case the ink stained only 75 % of the intertendinous segment of the subfascial part. In 57 % the subfascially applied ink penetrated the fascia and reached the subcutaneous compartment.
With US it is possible to examine and differentiate all segments of the SBRN. With US guidance it is possible to apply a fluid around the SBRN safely. If both, the subcutaneous and the subfascial compartment are targeted two needle placements would be needed as the forearm fascia forms an effective barrier for injected fluids. However, this cadaver study's results are to be confirmed by a clinical evaluation.

A 58 Cross-border mobility of junior neurologists within and to the European Union: an EAYNT survey

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Background: The mobility of medical doctors within and to countries of the European Union (EU) is steadily increasing and has already shown adverse effects on provision of medical service in some member states and regions.
Objective: To assess the general interest and motivation for cross-border mobility among residents and junior neurologists from member states of the EU and neighboring countries.
Methods: Questionnaire-based paper survey among 118 participants of a neurology course.
Results: Ninety-seven (82 %) returned the survey. Most of them had at one point considered to relocate within or to the EU for postgraduate education (87 %) or employment (71 %).
Common motivations were superior prospects for clinical training (85 %), resources at work and academic environment (both 80 %, respectively), and remuneration (70 %). Barely half of the surveyed intended to return to their home country. The attractiveness of Europe as a destination for migration was ranked over other continents. The most common reasons which repel from cross-border relocation were the loss of family connection (55 %) and uncertain future perspectives (41 %), whereas language barriers were less relevant (21 %).
Conclusion: There is keen interest of the upcoming generation of neurologists to relocate within and to the EU. The motives include regional divergent training and career opportunities, as well as economical welfare. Appropriate steps towards the harmonization of educational and career prospects are urgently required to ensure adequate provision of neurology service and patient care throughout Europe.

A 59 Considering transcallosal coherence as a marker of consciousness

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Question: Recent studies revealed differences in interhemispheric connectivity in disorder of consciousness (DOC)-patients. Based on this we investigate transcallosal coherence as a marker of consciousness. We compared Minimally Conscious States (MCS)-patients, Unresponsive Wakefulness Syndrome (UWS)-patients and healthy subjects (h). We assume to find greater coherence in healthy subjects than in DOC-patients and greater coherence in MCS- than in UWS-patients.
Methods: Rest-EEG was recorded in 66 subjects (24 MCS, 30 UWS, 12 Healthy). We computed the magnitude value of coherence between each electrode of the left hemisphere and each electrode of the right hemisphere (F3, F4, C7, F8, C3, C4, P3, P4, O1, O2). T-tests were calculated for each of the used 12 2.44 Hz frequency steps (1–28 Hz) and for each electrode combination between MCS- and UWS-group and between healthy subjects and DOC-patients.
Results: The statistics did not reveal remarkable differences between MCS- and UWS-patients. The comparison of DOC-patients and healthy subjects revealed statistical trends ($p<0.05$, uncorrected) in about 53.67 %

of the computed tests. We found an interesting pattern of common differences between DOC-patients and healthy subjects (H vs. MCS; H vs. UWS) in a frequency of 6 Hz.

Conclusions: The results indicate that the interhemispheric connectivity of MCS- and UWS-patients really do not differ systematically. Taken together this and the revealed differences between DOC-patients and healthy subjects, one might conclude that the impairment of consciousness in DOC-patients is based on a common mechanism to a certain extent. The earlier mentioned interesting pattern of common differences might reflect damage to frontal midline theta coherence, which in turn might reflect, regarding literature, an impairment of the working memory. It remains unclear which differences between MCS- and UWS-patients are responsible for behavioral differences.

A 60

Functional improvement in stroke patients in the subacute stage after treatment with whole-hand electrical stimulation

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Introduction: The present study examines the effect of whole-hand electrical stimulation on motor recovery in stroke patients at the subacute stage. Peripheral electrical stimulation has been proved to modulate cortical plasticity in healthy subjects and in patients. Such neuromodulatory effects have also been found after application of electrical hand mesh-glove stimulation (MGS) in our previous studies on healthy subjects.

Materials and methods: Patients with cortico-subcortical ischemic stroke and predominantly motor hemiparesis of the upper extremity were recruited for the study. MGS was applied on the paretic hand daily for 60 min before the standard rehabilitation training over three weeks. The hand motor and sensory functions were evaluated with Wolf Motor Function test, Fugl-Meyer Assessment score, Nine hole peg test, and Semmes-Weinstein monofilaments. Single and paired-pulse transcranial magnetic stimulation (TMS) was applied to follow the corticospinal excitability changes over the treatment period. Further, functional magnetic resonance imaging (fMRI) was conducted to assess the cortical brain reorganization changes after the treatment. Effects of MGS were compared to control group receiving sham stimulation.

Results: Patients form both groups showed significant functional improvement as assessed with the motor functional tests. However, the improvement degree for the MGS group was increased compared to the control group. These functional effects correlated with neuroplastic changes within the sensorimotor area as revealed by TMS and fMRI. Results will be reported at the DGNR meeting.

Discussion: Electrical stimulation applied before physiotherapeutic training raises the motor cortical excitability in the lessoned cortex so that the subsequent training becomes more effective. The obtained results provide better understanding of how modulation of central motor controlling structures by somatosensory stimulation correlates with the functional motor recovery.

A 61

Neurologische Leitsymptome in der interdisziplinären Notaufnahme des LKH St. Pölten

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Hintergrund: Neurologie ist ein eng an die Akutmedizin gekoppeltes Fach. Deshalb hat sich die integrierte neurologische Versorgung innerhalb von zentralen interdisziplinären Aufnahmestationen bzw. Notaufnahmen in vielen Krankenanstalten etabliert. Dies stellt die Grundlage für eine rasche und effektive diagnostische Abklärung akut neurologischer Fragestellungen dar. Der Anteil der über die Notaufnahme bzw. den Akut-Ambulanzbereich stationär aufgenommenen PatientInnen beträgt nach vorliegenden Daten zwischen 50 und 60 %.

Methodik: Modelhaft für unsere Untersuchung ist eine von Royl G. et al. 2010 vorgelegte Auswertung des akutneurologischen Patientenaufkommens an der Charité in Berlin. In der an unserem Zentrum durchgeführten Analyse wurden 4.300 PatientInnen aus dem Jahre 2011 retrospektiv erfasst, die in der Notfallaufnahme des Zentralklinikums St. Pölten primär bzw. konsiliarisch neurologisch begutachtet wurden.

Anhand der vorliegenden Triageprotokolle der Notfallaufnahme wurden die PatientInnen 12 verschiedenen neurologischen Leitsymptomen zugeordnet. Weiteres wurden in der Analyse akut durchgeführte diagnostische Maßnahmen, Transportmodalitäten zum Krankenhaus, der Zeitpunkt der Vorstellung, Alter, Geschlecht und der Wohnbezirk der PatientInnen berücksichtigt.

Ergebnisse: Der Anteil der PatientInnen mit neurologischen Fragestellungen im Rahmen der Notfallaufnahme des Zentralklinikums St. Pölten betrug im Jahr 2011 17 %. Das Durchschnittsalter der PatientInnen betrug 58 Jahre, das Geschlechterverhältnis 45 % (m) zu 55 % (w). Die häufigsten klinischen Leitsymptome waren Kopfschmerzen (20 %), Schwindel (19 %), motorisches Defizit (13 %) und epileptischer Anfall (7 %). Die höchsten Patientenfrequenzen konnten in der Zeit von 08:00 bis 19:00 Uhr (73 %) festgestellt werden. An neurologischen Zusatzuntersuchungen wurden am häufigsten CCT (47 %) und Duplexsonografien der extrakraniellen, hirnversorgenden Gefäße (12 %) durchgeführt.

Schlussfolgerungen: Die vorliegenden Daten lassen Rückschlüsse über die Bedeutung der zeit- und fachgerechten neurologischen Begutachtung in der Erstversorgung zu. Durch Etablierung konkreter Diagnosealgorithmen der wichtigsten Leitsymptome könnte sich die neurologische Akutversorgung weiter optimieren. Darüber hinaus liefern die Analysen der neurologischen Leitsymptome sowie des tageszeitlichen Aufkommens der PatientInnen wichtige Argumente hinsichtlich der personellen und technischen Ressourcenoptimierung.

Multiple Sklerose

A 62 Real life use of Natalizumab and Fingolimod in Austria: safety data from the Austrian Multiple Sclerosis Treatment Registry

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Background: High efficacy of Natalizumab and Fingolimod in the treatment of relapsing remitting multiple sclerosis (MS) has been proven in randomized trials. However, these do not necessarily reflect real-life situations faced in everyday practice. The Austrian MS Treatment Registry (AMSTR), established in 2006 and extended in 2011 to maintain quality control and comply with reimbursement regulations of the Austrian health authorities, allows obtaining such data, to assess indications, the clinical profiles of the treated populations and to monitor safety in real life.

Methods: The baseline documentation includes duration of disease, relapses within the last 12 months, EDSS, MRI activity and previous disease modifying therapies. Entry of follow-up data (relapses, EDSS, adverse events) is required in 3 months intervals. In addition, changes in treatment are documented. The statistical values below indicate means (range), unless otherwise indicated.

Results: As of January 14th 2014, 1164 patients treated with Natalizumab (70.2 % female) and 269 patients treated with Fingolimod (72.5 % female) have been registered. At baseline, their age was 35.5 (16–67) years in the Natalizumab and 38.4 (18–64) years in the Fingolimod group, with respective durations of the disease of 7.8 (0–40) years and 9.0 (0–32) years. The relapse rate in the year before the start of use of respective drugs was 2.3 (0–12) with Natalizumab and 1.8 (0–6) with Fingolimod. For those treated for at least one year, the subsequent relapse rates decreased to 0.36 (Natalizumab) and 0.42 (Fingolimod). At baseline, the EDSS was 3.2 (0–8.5) in the Natalizumab and 2.6 (0–7.5) in the Fingolimod treated group. EDSS stabilization or improvement was observed in 84 % (Natalizumab) and 80 % (Fingolimod). 38 % of the Natalizumab patients and 41 % of the Fingolimod patients stopped therapy according to the following reasons: patient's wish, adverse events (AEs), continuing disease activity, pregnancy or intended pregnancy. The most frequently reported AEs with Natalizumab were infections (n=72), general system disorders (n=51) and neurological disorders (n=51). Five cases of progressive multifocal leukoencephalopathy occurred so far among Austrian patients, which will be described in detail. In the Fingolimod group abnormalities of liver function (n=25) and hematology (n=14) and infections (n=10) were the most frequent AEs.

Conclusion: Over more than 7 years, the AMSTR has proved valuable to measure quality of care and monitor treatment, providing neurologists with highly relevant information in clinical routine. Continuous optimization and extension of this registry is a unanimous goal and necessity. Thus, new treatment modules are currently being developed and (external and independent) data monitoring and communication will be further improved. The availability of an increasingly broad treatment armamentarium with its consequences for daily routine practice (e.g. monitoring long-term benefit/risk profiles of individual drugs but also of their sequential use) emphasizes the need and the crucial importance of this registry for improved real life management of MS patients in Austria.

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A 63

Predictive value of different conventional and non-conventional MRI-parameters for specific domains of cognitive function in multiple sclerosis

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Objective: While many studies have correlated cognitive function with changes in brain morphology in multiple sclerosis (MS), few of them used a multi-parametric approach in a single dataset. Thus, we aimed to assess the predictive value of different conventional and quantitative MRI-parameters for both overall cognitive performance and specific domains of cognitive function in a sample of MS patients from a single centre.
Methods: 69 patients (17 Clinically Isolated Syndrome, 47 relapsing-remitting MS, 5 secondary-progressive MS) were assessed by the "Brief Repeatable Battery of Neuropsychological Tests" and underwent brain MRI at 3 T to obtain the following metrics: T2-lesion load (T2-LL), normalised brain volume (NBV), normalized cortical volume (NCV), normalized thalamic volume (NTV), normalized hippocampal volume (NHV), basal ganglia R2* values (iron deposition) and magnetization transfer ratios (MTR) for cortex and normal appearing brain tissue (NABT).
Results: Regression models including clinical, demographic variables and individual MRI-parameters explained 22–27 % of variance of overall cognitive performance, 17–26 % of cognitive efficiency and 22–23 % of memory. NCV T2-LL and NABT-MTR were the strongest predictors of overall cognitive function. Cognitive efficiency was best predicted by NCV, T2-LL and iron deposition in the basal ganglia. NTV and NHV were particularly related to memory function.
Conclusions: The predictive value of distinct MRI-parameters differs for specific domains of cognitive function, with a greater impact of cortical atrophy, focal and diffuse white matter abnormalities on overall cognitive function. An additional role of basal ganglia iron deposition on cognitive efficiency, and thalamic and hippocampal volume on memory function has been observed.
Keywords: cognition, cognitive efficiency, memory, normalized cortical volume, lesion load, quantitative MRI

A 64

Longitudinal changes of global and compartmental brain atrophy in patients with clinically isolated syndrome and clinically definite multiple sclerosis using 3-Tesla magnetic resonance imaging

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Background: Global and regional brain atrophy occurs very early in the disease course of multiple sclerosis (MS), but so far the clinical impact is still under discussion.
Aim: To determine the rate of brain atrophy in patients with a clinically isolated syndrome (CIS) suggestive of MS, compared to patients with clinically definite multiple sclerosis (CDMS) by long-term follow-up and to identify factors associated with more pronounced brain atrophy.
Methods: We investigated 63 CIS and 57

CDMS patients at baseline and after 3–4 years with detailed clinical examination and a comprehensive MR imaging protocol at 3 T. We assessed the annual change of brain parenchymal fraction (BPF) and of grey matter (GMF) and white matter (WMF) fractions, the percentage of brain volume change (PBVC) and change of T2 lesion load (T2-LL) with the support of semi-automated software (Siena and SIENAX and Display-image).

Results: The mean follow-up time was 42.5 months in CIS patients and 43.1 in CDMS patients (p=0.67). The mean age at baseline was comparable in both groups (CIS 32.6 yrs; CDMS 35.0 yrs; p=0.26). The mean annualised relapse rate was 0.23 in CIS and 0.29 in CDMS patients (p=0.162). Within a mean period of 21.1 months, 33 CIS patients (52.4 %) converted to CDMS.

At the baseline, BPF (p=0.018) and WMF (p=0.018) were significantly lower in CDMS patients. In contrast, the T2-LL in CDMS patients was significantly higher (p=0.003).

At follow-up CIS and CDMS patients had comparable rates of GMF (p=0.176), WMF (p=0.720) and BPF (p=0.526) changes. The PBVC was significantly higher in CDMS patients (p=0.001). Converters from CIS to CDMS showed a significantly higher PBVC than non-converters (p=0.029).

In the total cohort PBVC correlated with the annualised relapse rate (r=0.208; p=0.023), the expanded disability status scale (EDSS) (r=0.201; p=0.028) and the T2-LL at baseline (r=0.25; p= 0.005).

Conclusion: Conversion from CIS to CDMS is associated with a similar global brain atrophy rate despite shorter disease duration. Compartmental brain atrophy occurs in CIS at a similar rate as in CDMS.This confirms the importance of brain volume changes in the surveillance of the evolution of the disease already in the early stage of MS.

A 65

The default mode network – the resting-state network most sensitive for cerebral functional changes over short-term in multiple sclerosis

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Applying resting state functional MRI (RS-fMRI) in patient cohorts bears great potential for exploring functional cerebral reorganization with progression of CNS disorders, obviating the influences of performance bias associated with task-related fMRI. However, the analysis of such datasets is demanding and studies using such an approach in a longitudinal manner are scarce. Given the dynamics of the disease, multiple sclerosis (MS) represents an attractive candidate to test the feasibility of longitudinal RS fMRI to explore such changes over short-term. For this purpose, we selected two patient groups, 9 MS patients on conventional disease-modifying treatment (DMT; glatiramer acetate or ß-interferons) and 11 MS patients with active disease in whom Natalizumab treatment had been initiated recently (NAT). Participants underwent structural, functional MRI, neurological and neuropsychological examinations at baseline (BL) and at 3 months of follow-up (FU).

In line with the literature, at BL, we succeeded in identifying nine networks in both groups, without any differences between groups. At FU, significant changes had occurred in exclusively one out the nine networks, i.e. the default mode network (DMN). Functional increases were greater in the DMT group than in the NAT group, comprising the anterior and posterior cingulate, the middle frontal gyrus, the supramarginal gyrus, the occipital pole, and the cerebellum.

This study demonstrates that changes in RS activation in MS may already be captured over short-term. The stability (and thus reproducibility) of all but one RS networks attests to the validity of the analytical approach used. Consistent with the notion of the DMN as a critical functional hub sensitive to changes in brain integrity, the only changes observed affected the DMN changes, suggesting its potential relevance for sensitive monitoring of disease evolution in MS.

A 66

Zurückgezogen

A 67

Ein neues Tiermodell der fokalen entzündlichen Demyelinisierung im Neokortex der Ratte

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Die experimentelle Autoimmun-Enzephalomyelitis (EAE) ist ein weit verbreitetes Tiermodell der Multiplen Sklerose im Nagetier; die damit im Versuchstier erzeugten Läsionen zeigen eine Vielzahl an histopathologischen Merkmalen der Multiplen Sklerose. Dennoch bestehen einige wichtige Unterschiede: Einerseits betreffen die Läsionen überwiegend die unteren Rückenmarksabschnitte und nur sehr selten kortikale Regionen. Zudem ist die exakte Lokalisation, wo genau eine Läsion entstehen wird, nicht genau vorhersehbar. Wir präsentieren eine neue Methode, mittels eines implantierten Kathetersystems („cerebral open flow microperfusion", cOFM) reproduzierbare fokale entzündlich-demyelinisierende Läsionen im Neokortex der Ratte zu erzeugen. Die cOFM ist eine minimalinvasive Technik, bei der ein Kathetersystem direkt in den Neokortex der Ratte implantiert wird; das Material des Katheters ist so gut gewebeverträglich, dass auch bei wochenlanger Liegedauer keine Abwehrreaktion des Gewebes im Sinne einer Glianarbenbildung entsteht und damit jederzeit Zugang zu intaktem Hirngewebe gewährleistet ist. Nach einer Einheilungsphase können Flüssigkeiten über das Kathetersystem kontinuierlich eingespült werden. Auch das Entnehmen von Proben für weiterführende Untersuchungen ist jederzeit möglich. Zwei Wochen nach Implantation des Katheters werden die Ratten subklinisch mit 100 µg MOG (Myelin-Oligodendrozyten-Glykoprotein) in inkompletten Freund's Adjuvant subkutan immunisiert. Nach Erreichen eines stabilen Antikörpertiters gegen MOG wird ein Zytokincocktail aus 250 ng rekombinantem TNF-alpha und 150 U IFN-gamma über den cOFM-Katheter ins Gehirngewebe eingespült. Dies führt zu einer selektiven Öffnung der Blut-Hirn-Schranke, einem Einstrom der Anti-MOG-Antikörper aus dem Blut und in weiterer Folge der Bildung einer entzündlich-demyelinisierenden Läsion um die Katheterspitze.

Zusammenfassung: Unsere neue Methode ermöglicht es uns, reproduzierbare entzündlich-demyelinisierende Läsionen im Neokortex der Ratte zu erzeugen. Diese bleibt klinisch stumm und daher sind auch lange Überlebenszeiten zur Untersuchung auch später Läsionsstadien ethisch vertretbar. Das Kathetersystem erlaubt jederzeit Zugriff zur Läsion zwecks Probenentnahme von Gewebsflüssigkeit für weitere Untersuchungen bzw. zum Einspülen experimenteller Testsubstanzen.

A 68

Natalizumab and fingolimod differentially impact the alpha-4/beta-1 expression-related subset diversity of T cells

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Background: The alpha-4/beta-1 integrin is crucially involved in the transmigration of immune cells across the blood-brain barrier into the central nervous system. Natalizumab and fingolimod are two effective treatment options in relapsing-remitting multiple sclerosis (RRMS). Natalizumab blocks alpha-4, whereas the main effector mechanism of fingolimod is to trap lymphocytes in lymph nodes after homing. Here we report about the differential impact of fingolimod and natalizumab on the alpha-4/beta-1-related subset diversity of T cells in the peripheral blood.

Methods: Coexpression of alpha-4 (anti-CD49d-PE, clone 9F10) and beta-1 (anti-CD29-FITC, clone 4B4) on naive and memory CD4+ and CD8+ T cells was investigated by flow cytometry. Peripheral blood mononuclear cells from 10 RRMS patients were analyzed prior to (T0) and after 3 months of treatment (T1) with natalizumab (n=5) or fingolimod (n=5).

Results: Analyzing the coexpression of alpha-4 and beta-1 at baseline revealed two subsets (alpha-4$^+$/beta-1^{low}, alpha-4+/beta-1$^+$) of naive CD4+, naive CD8+, and memory CD8+ T cells, and a third subset (alpha-4–/beta-1+) of memory CD4+ T cells. Natalizumab treatment led to a pronounced decrease of the alpha-4$^+$/beta-1^{low} subsets of naive CD4+ (T0:77±10 %; T1:17±9 %; p<0.001) and CD8+ (T0:67±21; T1:21±6; p<0.01) T cells and to a reduced frequency of the alpha-4$^+$/beta-1$^+$ subsets of memory CD4+ (T0:62±8 %; T1:48±10 %; p<0.05) and CD8+ (T0:60±5; T1:39±8; p<0.05) T cells. Differently, fingolimod treatment led to an increased frequency of alpha-4+/beta-1+ subsets of naive CD4+ (T0:23±10 %; T1:47±14 %; p<0.05) and CD8+ (T0:38±13; T1:59±6; p<0.05) T cells. The frequency of the alpha-4$^+$/beta-1$^+$ memory CD4+ and CD8+ T cell subsets remained largely unchanged.

Conclusion: Natalizumab acts as a brake on the alpha-4 expression resulting in reduced frequencies of alpha-4/beta-1 coexpressing T cell subsets. The fingolimod-mediated redistribution of immune cells rather leads to a relative increase in the frequencies of naive alpha-4$^+$/beta-1$^+$ T cells. This raises the question if an extensive subset analysis between patient groups might allow differentiating disease-promoting cells from those required for immune surveillance.

A 69 Dynamics of brain iron accumulation differ between clinically isolated syndrome and multiple sclerosis: a longitudinal 3 T MRI study

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Introduction: Increased iron concentration in cerebral deep gray matter is a consistent finding in multiple sclerosis (MS), while respective results have been controversial in patients with a clinically isolated syndrome (CIS). This suggests a temporal dynamic of iron accumulation. We therefore attempted to investigate this process and its relation to other brain morphologic findings by a long-term follow-up of CIS and MS patients.
Subjects and methods: We studied 76 patients with CIS and 67 with MS with baseline and follow-up 3 T MRI and detailed clinical examination. Iron deposition in subcortical gray matter structures (caudate nucleus, globus pallidus, putamen and thalamus) was assessed by automated, regional calculation of R2* rates. We further determined T2 lesions load and percentage of brain volume change (PBVC).
Results: The age of CIS and MS patients was comparable (mean CIS 32.0 yrs SD 8.3, MS 34.2 yrs SD 9.3, p=n.s.) as was the median duration of MRI follow-up (CIS 2.6 yrs, MS 3.0 yrs; p=n.s.). Median disease duration was significantly higher in MS (CIS 0.3 yrs, MS 7.5 yrs; p<0.001).
At baseline, R2* relaxation rates were significantly higher in MS compared to CIS regarding all basal ganglia structures (p<0.01), but not in the thalamus (p=n.s.).
In CIS, R2* relaxation rates significantly increased over time in the globus pallidus (p<0.001), putamen (p<0.001) and the caudate nucleus (p<0.01), but not in the thalamus. In contrast in MS, R2* rates only slightly increased in the putamen (p<0.05), remained stable in the globus pallidus and caudate nuclei and significantly decreased in the thalamus (p<0.001). Using a hierarchical regression analysis controlling for age, disease duration and MRI follow-up time, the change of R2* rates over time within the globus pallidus was an independent predictor of increasing brain atrophy (PBVC) in CIS (β=0.4, p<0.05) but not in MS. There were no correlations with the change in other morphologic variables.
Conclusion: Iron accumulation is an early phenomenon of the disease, which parallels brain volume loss and appears to plateau over time. These dynamics suggest that higher iron concentration in MS is a consequence of ongoing morphologic damage. Whether increased iron concentration exerts detrimental effects of its own or not, deserves separate investigation.

A 70 Changes to anti-JCV antibody index during natalizumab therapy in an Austrian MS cohort

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Background: Presence of anti-JC virus antibodies (anti-JCV-Ab) is a risk factor for progressive multifocal leukoencephalopathy (PML) in natalizumab (NAZ)-treated multiple sclerosis (MS) patients. A recent study showed that an anti-JCV-Ab index above >1.5 (no prior immunosuppressive treatment of patients presupposed) correlated with an increased PML risk.
Objective: To longitudinally explore the development of anti-JCV-Ab index-based results in an Austrian MS cohort.
Methods: Anti-JCV-Ab serostatus and anti-JCV-Ab index were determined by Unilabs Denmark with the second-generation assay

STRATIFY JCV DxSelect™ (Focus Diagnostics, Cypress, California). 53 MS patients with their sera analyzed twice, for the first time prior to the start treatment and a follow-up sample during NAZ, and one PML case lacking a pre-treatment sample were included in this analysis. Positive anti-JCV-Ab index results were categorized low risk if <1.5 or high risk if >1.5.

Results: From the 53 MS patient 19 (36 %) were anti-JCV-Ab seropositive and 34 (64 %) were seronegative before natalizumab therapy was initiated. Of the JCV-Ab seropositive group, 10 patients were categorized low risk (<1.5) and 9 patients were categorized high risk (>1.5). At the follow-up measurement during natalizumab treatment, a dynamic was observed in the development of the anti-JCV-Ab index in 15 (28 %) patients. A seroconversion from negative to positive was seen in 9 patients including one who directly converted into the high risk group. A switch from the low risk into the high risk group was observed in 6 out of 10 patients (60 %) with an initial index <1.5. Both serum samples of the PML patient had an anti-JCV-Ab index >1.5.

Conclusion: Our data indicate a dynamic of the anti-JCV-Ab index between the pretreatment samples and the follow-up samples collected during NAZ treatment. Changes were seen in seropositive as well as in seronegative patients. We conclude that continued measurements are important in all patients to keep track on a possible switch into another risk group. Nevertheless, the impact of a change in the risk category of an individual patient remains to be elucidated.

AZ1

Use of peripheral blood mononuclear cells of interferon-ß-1b-treated multiple sclerosis patients for permeability assay in an in vitro blood-brain barrier model

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Background and objective: The exact molecular mechanisms leading to an improved disease course in interferon beta (IFN-β)-treated multiple sclerosis (MS) patients are not yet completely understood. Recently, a stabilizing effect of serum from IFN-β-1b-treated patients on an in vitro blood-brain barrier (BBB) model was shown (Müller et al. 2010). With the intention to develop a bioassay for treatment response, we investigated the effect of peripheral blood mononuclear cells (PBMC) from IFN-β-1b-treated MS patients on the paracellular permeability of an in vitro BBB.

Method: The in vitro BBB model consisted of immortalized human microvascular endothelial cells (iHBMEC) cultured in rat astrocyte-conditioned medium. Permeability for 3H-Inulin and 14C-Sucrose across iHBMEC monolayers was assessed after an overnight challenge with PBMC from untreated (baseline) and short-term (3 months) IFN-ß-1b-treated MS patients (n=9), from long-term (median 8 years, range 2–15) IFN-β-1b-treated MS patients (n=12), and from healthy controls (n=9).

Results: Addition of PBMC resulted in an increased paracellular permeability of iHBMEC monolayers compared to medium. There were no differences, however, in paracellular permeability read-outs between PBMC from untreated MS patients, short- or long-term IFN-ß-1b-treated MS patients, or healthy controls.

Discussion: Differential effects on BBB permeability between PBMC from untreated patients, IFN-β-1b-treated patients or healthy controls were not observed. This shows that PBMC are not qualified for in vitro set-up using paracellular permeability as outcome measures. The usefulness of employing patient PBMC in a transmigration-based BBB system as bioassay for IFN-β treatment response remains to be determined.

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A 72

A routine-qualified flow cytometric method for the identification of multiple sclerosis patients with a reduced therapeutic effectiveness of natalizumab

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Background: Natalizumab (NZB)-neutralizing antibodies (NAB) occur in 9 % of NZB-treated multiple sclerosis (MS) patients. Loss of clinical and biological efficacy in patients with persisting NAB requires termination of NZB treatment.

Objective: Since high-titer NAB are strongly associated with persistence of NAB, we investigated if determination of NZB saturation levels of alpha-4 integrins by flow cytometry has the potential to early identify patients with NAB.

Methods: Cell-bound NZB and NZB saturation of alpha-4 integrins on T cells were detected by flow cytometry using a monoclonal anti-human IgG4 antibody. Peripheral blood mononuclear cells were enriched from venous blood collected at the start (baseline) and every 4 weeks immediately before subsequent infusions until up to 9 months from NZB-treated patients with NABs (n=4) and at the start and after 1 (n=15), 2 (n=14), 3 (n=9), 6 (n=7), and 9 months (n=3) from NZB-treated patients without NABs. NZB saturation level (in %) of T cells was determined by relating median fluorescence intensities (MFIs) of in vivo bound NZB to MFIs after in vitro incubation with saturating amounts of NZB. Determination of serum NABs was performed by ELISA.

Results: In patients without NABs, the median NZB saturation level of T cells over 9 months was 75 % (confidence interval of 95 %: 72–78 %). In two of the four patients with NABs, NZB saturation level of T cells only reached approximately 50 % after the first infusion and further declined to baseline levels with the second infusion. Low-titer NABs were measured after the first infusion and development of persistent high-titer NABs led to termination of NZB treatment after 6 months. In another two patients, NZB saturation level of T cells was 74 % and 68 % after the first infusion, temporarily decreased to approximately baseline levels and re-increased after approximately 6 months. Transient NABs were detected after 2 and 3 months, which resolved after 5 and 6 months.

Conclusions: Monitoring NZB saturation level on T cells is a fast and reliable method to identify patients with a reduced treatment effect due to NABs. Both high- and low-titer NABs were equally effective in reducing cellular NZB saturation level. We were able to show that NZB saturation level, as detected by flow cytometry, is a sensitive method for detecting a prolonged NAB-mediated reduced treatment effect because NABs are apparently effective longer than suggested by the detection limit of ELISA.

A 73 *Unusual deterioration in a multiple sclerosis patient on natalizumab therapy: not always PML*

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Background: Whenever multiple sclerosis (MS) patients on natalizumab therapy develop atypical neurological symptoms, progressive multifocal leukoencephalopathy (PML) has to be excluded. We here describe a case of a patient with MS receiving natalizumab for 5 years, suspected to have PML and finally diagnosed with Creutzfeldt Jakob disease (CJD).

Case report: This is a case report of a 42-year-old woman with known MS for more than 15 years, who was admitted to a university clinic because of rapidly progressive neuropsychological deficits and ataxia, initially suspected to suffer from PML. She had been treated with natalizumab for 5 years and had a seroconversion to JC virus antibody positivity. However, clinical work-up including magnetic resonance imaging, lumbar puncture, repeated electroencephalography and blood testing ruled out PML and led to the diagnosis of probable sporadic CJD. One month after hospital discharge, the patient died and the diagnosis was confirmed by brain autopsy.

Conclusion: Increased vigilance and a diligent work-up of differential-diagnoses are demanded in MS patients who develop unusual symptoms and signs under therapy.

A 74 *Multiple-Sklerose-Läsionen in der diffusionsgewichteten Messung im Schub und im schubfreien Intervall*

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Einleitung: Akute MS-Läsionen können aufgrund eines vasogenen Ödems in der Diffusionsbildgebung häufig einen T2-Durchscheineffekt mit erhöhtem ADC-Signal („apparent diffusion coefficient") aufweisen (Balashov et al. 2011). Ähnlich einer rezenten Ischämie werden zusätzlich bei akuten MS-Läsionen Diffusionsstörungen mit verminderter ADC beschrieben, welche etwa 1 Woche in dieser Form bestehen bleiben, danach kommt es zu einer Normalisierung bzw. Erhöhung des ADC (Eisele et al. 2012).

Methodik: Die primäre Fragestellung in dieser Arbeit war, die Häufigkeit von T2-Durchscheineffekten und Diffusionsstörungen bei MS-Patienten im Schub und im schubfreien Intervall zu eruieren. Sekundär wurden weitere MRT-Parameter wie Anzahl und Lokalisation der Plaques und Kontrastmittel-Enhancement (KME) evaluiert. Zu diesem Zweck wurde die MS-Datenbank des

AKH Linz retrospektiv auf Patienten mit einer MRT-Untersuchung einschließlich Diffusionsmessung bis zu 30 Tage nach Schubbeginn und im schubfreien Intervall durchleuchtet. Dabei fanden sich 38 Datensätze mit den erforderlichen MRT-Kriterien im Schub und 34 im schubfreien Intervall. Bei 12 Patienten gab es Datensätze im Schub sowie im schubfreien Intervall.

Ergebnisse: In beiden untersuchten Gruppen konnte keine Diffusionsstörung nachgewiesen werden. Unterschiede ergaben sich in Bezug auf KME (53 % vs. 38 %) und T2-Durchscheineffekt (61 % vs. 18 %) mit Überwiegen in der Schub-Patienten-Gruppe. Insgesamt zeigten die Schub-Patienten mehr Plaques (68 % vs. 42 % > 10 Plaques). Hauptsächlich lagen die Plaques supratentoriell (95 %), bei 28 % davon waren sie zusätzlich infratentoriell lokalisiert. Bei der Mehrheit der Patienten (65 %) waren die Plaques periventrikulär angeordnet.

Konklusion: Wie in der Literatur vorbeschrieben (Balashov et al. 2011) treten auch in unserer untersuchten Population im akuten Schub vermehrt T2-Durchscheineffekte auf. Eine Diffusionsstörung hingegen ist nicht aufgetreten. Diese Tatsache dürfte einerseits auf das seltene Auftreten derselben (Balashov et al. 2012; Eisele et al. 2012) und andererseits auf das begrenzte Zeitfenster nach Schubbeginn (1 Woche) zurückzuführen sein (Eisele et al. 2012).

A 75

Delayed third degree atrioventricular block with pacemaker placement in a multiple sclerosis patient on fingolimod treatment

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Objective: To report a serious cardiac adverse event in a patient with multiple sclerosis (MS) after 14 months on fingolimod.

Background: Fingolimod is approved for the treatment of MS and well known to cause transient bradycardia and first/second degree atrioventricular block (AV) after the first dose. There were no fatal cardiac complications in the pivotal clinical trials; however, cases of sudden or unexpected deaths were registered in the postmarketing setting.

Case report: The patient developed first symptoms of MS retrospectively at age 55. The diagnosis was made at age 61 and supported by a brain biopsy. Interferon-1b was started five months later. The medical history for cardiovascular disorders was unremarkable; risk factors included smoking (40 py). Persistent clinical and radiological disease activity over the next 12 months required escalation therapy with fingolimod 0.5 mg (EDSS 2.0, JCV seropositivity). Cardiac monitoring at treatment initiation and follow-ups were unremarkable. Despite excellent adherence he had sustained clinical and radiological disease progression. After 14 months on fingolimod, he presented with shortness of breath and reduced physical fitness. The ECG revealed a third degree AV block (35 bpm) and ventricular rhythm with an intermittent right bundle branch block-like QRS-complex. There was no evidence of a structural heart disease. Immediate cessation of fingolimod and medical treatment did not lead to restoration of the heart rate and a DDD(R) pacemaker was implanted three days later. One week later, he developed a severe relapse attributed to a brainstem lesion (EDSS 5).

Conclusion: Recent case studies, including ours, point at potential late occurrence of life-threatening cardiac side effects in patients on fingolimod. We bring up three hypotheses for discussion: autonomic dysfunction related to the relapse, adverse event associated with fingolimod treatment, or most likely, a combination of both. Hence, surveillance for similar incidents should continue to identify additional risk factors for cardiac adverse events.

A 76

Excellent outcome in natalizumab-associated PML due to early diagnosis and optimal treatment

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Objective: To underline the importance of early diagnosis and proper treatment for a good outcome in MS patients with natalizumab-associated PML.

Background: PML is a rare but severe complication during natalizumab treatment. Due to its efficacy natalizumab remains an important therapeutic option in patients with an increased risk of developing PML.

Design/Methods: case report

Results: We report about a 43 years old male JCV seropositive MS patient on natalizumab treatment since 2007. An increase in gait disturbance in 02/2013 was the reason for admission to our hospital. MRI revealed an atypical lesion in the cerebellum. Detection of JCV DNA in the cerebrospinal fluid (CSF) by PCR led to the diagnosis of natalizumab-associated PML. Immune phenotyping showed the typical inversed CD4/CD8 T cell ratio in the CSF reflective of natalizumab effects behind the blood-brain barrier.

Serial plasma exchange (PLEX) was performed to accelerate immune reconstitution. Natalizumab desaturation of lymphocytes was monitored by flow cytometry. Eight cycles of PLEX were necessary for sufficient natalizumab clearance from the blood which was also confirmed by ELISA. MRI six days after the last PLEX was indicative of an incipient immune reconstitution inflammatory syndrome (IRIS). CSF showed a slight pleocytosis, normalized CD4/CD8 T cell ratio and very low residual levels of free natalizumab indicating that the blocking effect of natalizumab was abrogated. IRIS was treated with high dose methylprednisolone. The patient was clinically stable during the entire period and the initial gait disturbance diminished after a few weeks.

Conclusion: The most important factors for a good outcome of natalizumab-associated PML are early diagnosis, immediate reconstitution of the immune system, and control of IRIS. They depend on tight clinical patient surveillance, sufficient PLEX treatment and an early counter to IRIS. Serial flow cytometric analyses of blood and CSF can assist in evaluating the effect of PLEX and timing of when to counteract IRIS.

Muskelerkrankungen

A 77 Increased prevalence of malignancy in mitochondrial disorders

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Objectives: There are indications that patients with a mitochondrial disorder (MID) develop more frequently malignomas or benign tumours than the general population. Aims of the study were to find out if the prevalence of tumours is actually increased in MID-patients and which of the malignomas or benign tumours are the most frequent.
Methods: Retrospectively evaluated were the charts of MID-patients for the presence of malign or benign tumours. MID was diagnosed according to the modified Walker-criteria.
Results: Among 475 MID-patients screened for tumours, at least a single malignoma was found in 65 patients (13.7 %), and at least a single benign tumour in 35 patients (7.4 %). Among those with malignancy, 22 were men and 43 female. Among those with a malignancy 1 had definite MID, 9 probable MID, and 55 possible MID. The most common of the malignancies was breast cancer, followed by dermatological, gynecological, and gastrointestinal malignancies. The most frequent of the benign tumours was lipoma, followed by pituitary adenoma, meningeomas, carcinoids, and suprarenal adenomas. Compared to the general population, the prevalence of malignancies and of benign tumours was markedly increased. The female preponderance was explained by the frequent maternal inheritance of MIDs.
Conclusions: Adult patients with a MID, particularly females, carry an increased risk to develop a malignancy or a benign tumour. Since malignancy is an important determinant for their outcome, these patients should be more accurately screened for neoplasms, not to overlook the point, at which an effective treatment can no longer be provided.

A 78 Distal myosin heavy chain-7 (thumb) myopathy due to the novel transition c.5566G>A with heterogeneous cardiac involvement

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Objectives: Myosin-heavy-chain (MYH7)-myopathy manifests clinically with a distal, scapuloperoneal, limb-girdle (proximal), or axial distribution and may involve the respiratory muscles. In the majority of the cases the heart is affected, ranging from relaxation impairment to dilative cardiomyopathy with ventricular arrhythmias. Progression of cardiac involvement and earlier onset in successive generations has not been reported in MYH7-myopathy.
Case study: In a five-generation family

MYH7-myopathy manifested with late-onset, distal > proximal myopathy and variable degree of cardiac involvement. The index patient developed myopathy from age 49 y with anginal chest pain. Her mother presented with a similar phenotype but had only developed myocardial relaxation impairment. The daughter of the index patient had only mild distal myopathy but presented with left ventricular hypertrabeculation/noncompaction and required an implantable cardioverter defibrillator (ICD) because of ventricular arrhythmias since age 37 y. Her daughter was diagnosed with dilated cardiomyopathy at infancy, without overt skeletal muscle disease. MYH7-myopathy in the presented family was due to the novel mutation c.1566G>A in the MYH7 gene.

Conclusions: There is cardiac involvement in MYH7-myopathy, and cardiac affection in MYH7-myopathy is highly variable between the generations ranging from relaxation abnormality to noncompaction, ventricular arrhythmias, and dilated cardiomyopathy. While manifestations and progression of MYH7-myopathy may be mild, cardiac disease in MYH7-myopathy may be highly variable and progress with successive generations.

Key words: neuromuscular, myopathy, skeletal muscle, genetics, cardiac involvement, cardiomyopathy, arrhythmias, noncompaction, myosin heavy chain

A 79

Distal MYH7 (thumb) myopathy due to the novel transition c.5566G>A with marked cardiac phenotypic heterogeneity

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Objectives: MYH7-myopathy manifests clinically with a distal, scapuloperoneal, limb-girdle (proximal), or axial distribution and may involve the respiratory muscles. In the majority of the cases the heart is affected, ranging from relaxation impairment to dilative cardiomyopathy (dCMP) with ventricular arrhythmias. Progression of cardiac involvement and earlier onset in successive generations has not been reported in MYH7-myopathy.

Case study: In a four-generation family MYH7-myopathy manifested with late-onset, distal>proximal myopathy and variable degree of cardiac involvement. The index patient developed myopathy from age 49 y with anginal chest pain. Her mother presented with a similar phenotype but had only developed myocardial relaxation impairment. The daughter of the index patient had no overt myopathy but presented with left ventricular hypertrabeculation/noncompaction and required an ICD because of ventricular arrhythmias since age 37 y. Her daughter was diagnosed with dCMP at infancy, also without overt skeletal muscle disease. MYH7-myopathy in the presented family was due to the novel mutation c.1566G>A in the MYH7 gene.

Conclusions: There is cardiac involvement in MYH7-myopathy, and cardiac affection in MYH7-myopathy is highly variable between the generations ranging from relaxation abnormality to noncompaction, ventricular arrhythmias, and dCMP. Cardiac disease in MYH7-myopathy seems to progress with successive generations.

PNS

A 80 Neuroimaging in thoracic outlet syndrome caused by cervical ribs

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Background: Neurogenic thoracic outlet syndrome (nTOS) is a complex disorder that often imposes difficulty in diagnosis as symptoms can be subtle and unspecific. Cervical ribs are a well-known cause of nTOS, but relation between the bony and nerval structures could not be assessed until now. Progress of MRI and high-resolution ultrasound (HRUS) now opens up new opportunities in visualization of nerval tissue and its spatial relation to bony structures. Additionally, HRUS can be used for sonopalpation to confirm triggering of symptoms by applying local pressure, functional assessment and HRUS-guided blockade for confirming resolution of symptoms.

Methods: We reviewed the Radiologic Information System for patients with the final diagnosis of non-specific or neurogenic TOS caused by cervical ribs within the time frame of the last 24 months, that underwent HRUS (GE Logic E9, ML 6-15-D and L8-18i-D) and MRI (3 Tesla, specific sequences) at our department.
Sonopalpation, functional assessment and selective blockade of nerve roots presumed to be causative for symptoms were performed in all patients.

Results: Six patients were assessed for suspected nTOS or non-specific TOS and turned out to have a cervical rib, one also showing a pseudarthrosis with the first rib. The cervical roots and their relation to the rib could be visualised by HRUS and MRI, showing a riding of root C6, C7 or C8 in all patients, with traction of roots when turning the head. Sonopalpation was positive in all patients, producing paraesthesias of different pattern radiating down the arm. Selective blockade brought temporary resolution of pain in all patients.

Conclusion: HRUS and MRI can visualize nerval and bony structures in patients with suspected nTOS. Additionally, HRUS can be used for sonopalpation, functional assessment and selective blockade. These imaging modalities are helpful in diagnosing nTOS and non-specific TOS.

A 81 Acute intermittent porphyria (AIP) presenting as acute neuropathy, a laboratory and genetically confirmed observation

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Introduction: AIP is an inherited metabolic disorder and is one of the main differential diagnosis for acute motor neuropathy.

Methods: Single case report.

Case report: We report a 32 years old previously healthy female patient presenting with recurrent heavy abdominal pain since 2 months. A urinary tract infection and a polycystic ovary syndrome had been considered. Antibiotics and analgesics had been given without success. In the course of weeks the patient had lost

weight (11 kg) and developed a general weakness.

At admission, the patient had a progressive proximal symmetrical flaccid tetraparesis (BMRC 3 prox., 4 dist.), normal tendon reflexes and no sensory loss. However, she reported about general hyperalgesia and diffuse pain. Severe tachycardia was considered to be a sign of autonomic involvement. The tetraparesis progressed within 4 days (BMRC 1 prox., 2 dist.). Due to the combination with abdominal symptoms we suspected AIP and initiated continuous IV application of glucose and repeated hematin therapy.

Over 2 months the patient gradually recovered (BMRC 3 prox., 4 dist.) and was transferred to a rehab centre.

Findings: Laboratory:

- 24-hour urine analysis: porphyrin (3300 µg; <150 µg), aminolevulinic acid-U (90 mg/l; <10 mg/l) and porphobilinogen (142 mg/l; <1,7 mg/24 hr)
- Genetic examination: confirmation of AIP (mutation c.973C>T). Family history for AIP was negative.
- NCV: mild axonal neuropathy with preserved sensory conduction velocities; F-waves preserved
- EMG: no denervation, mild myopathic signs in the right deltoid muscle
- SSEP, MEP: normal
- Cerebral MRI: normal

Discussion: This is a case report of a family negative AIP presenting with an acute motor neuropathy and abdominal symptoms. AIP is an inherited metabolic disorder of hem synthesis resulting in a decreased activity of uroporphyrinogen-I-synthesis. This evokes an accumulation of porphyrin precursors which toxically influence the nervous system. More often women are affected and the onset is usually post puberty until the 5th decade. An initial symptom is often abdominal pain followed by symmetric or asymmetric neuropathy with proximally accentuated tetraparesis. Tendon reflexes may be reduced. A diffuse pain syndrome, autonomic symptoms, mental state changes and seizures are reported. The duration of an attack may be days to weeks, usually with a complete recovery. Treatment consists of hematin, which suppresses symptoms of acute attacks. Patients have to be advised to avoid extreme fasting and certain drugs.

Conclusion: Therapy-refractory abdominal pain combined with general weakness has to be considered as differential diagnosis for AIP. Rapid progression and severe tetraparesis with almost normal electrophysiology are possible. In our patient with delayed diagnosis only a slow and incomplete recovery despite intensive therapy was seen. Early diagnosis and therapy initiation is important.

A 82

Nicht immer sind Polyneuropathien für Fußschmerzen verantwortlich

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Hintergrund: In rezenten Publikationen wird eine Zentralisierung des Schmerzes bei Arthrosen beschrieben. Als Ursache werden einerseits die chronische Reizung der Nozizeptoren, andererseits neuropathische Schmerzmechanismen angesehen[1, 2]. Wir berichten von einem Patienten, der im Rahmen einer dialysepflichtigen Niereninsuffizienz eine Osteoarthropathie entwickelte und zunächst als renale Polyneuropathie eingestuft wurde.

Fallbericht: Ein 71-jähriger Mann mit einer dialysepflichtigen chronischen Niereninsuffizienz entwickelte in den letzten 6 Monaten heftige und belastungsabhängige Schmerzen in beiden Vorfüßen. Der Schmerzcharakter wurde vom Patienten als brennend und stechend angegeben. Beim Gehen kam es zu einer deutlichen Schmerzverstärkung.

In der klinisch-neurologischen Untersuchung zeigten sich beidseits fehlende Achillessehnenreflexe bei grob intakter Sensibilität und reduziertem Vibrationsempfinden (6/8). Auffallend war links eine Schwellung des Sprunggelenkes. Die NLG ergab beidseits eine milde axonale Neuropathie (NCV 35 m/s) und eine erniedrigte Amplitude des N. suralis. Bei der quantitativen sensorischen Testung (QST) zeigte sich am linken Fußrücken eine deutliche Verzögerung der Kalt- und Warmempfindung. In einer MRT-Untersuchung der Sprunggelenke wurde eine Osteoarthropathie mit Knochennekrosen und Markraumödem diagnostiziert. Nach analgetischer Therapieoptimierung, lokalen orthopädischen Therapien und auch im Gefolge der Nierentransplantation konnte eine Schmerzreduktion erzielt werden.

Diskussion: Renale Osteoarthropathien sind seltene und schmerzhafte Komplikationen bei renaler Insuffizienz. Sie sind belastungsabhängig schmerzhaft und gehen mit Ergüssen und hochgradigen Veränderungen im Gelenk einher. Klinisch hinweisend war die starke Belastungsabhängigkeit der Beschwerden, die zeitweise zur Immobilität führte. Die konventionelle NLG und die QST bestätigten zwar das Vorliegen einer axonalen PNP und vermutlich auch einer Kleinfaserneuropathie, konnten aber die Beschwerden nicht ausreichend erklären.

Therapeutisch konnte sowohl durch lokale orthopädische Maßnahmen als auch in der Folge durch Besserung der renalen Situation nach Nierentransplantation Besserung erzielt werden.

1 Suokas AK et al., Quantitative sensory testing in painful osteoarthritis: a systematic review and meta-analysis. Osteoarthritis Cartilage 2012 Oct; 20(10):1075–85
2 Soni A et al., Neuropathic features of joint pain: a community-based study. Arthritis Rheum 2013 Jul; 65(7):1942–9

Schlaganfall

A 83 Thrombektomie bei Karotis-T-Gabelverschluss – Outcome-Analyse von 33 Fällen

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Hintergrund: Ziel der akuten Schlaganfallbehandlung ist eine rasche Gefäßrekanalisation und damit eine Reduktion von Behinderung und Mortalität. Ein guter Rekanalisationserfolg mit intravenöser rTPA kann nur bei kleinen Hirngefäßen erzielt werden. Bei thrombembolischem Verschluss großer Gefäße ist der Therapieerfolg sehr gering. Bei Patienten mit proximalen Gefäßverschlüssen und großem Thrombenvolumen besteht durch die endovaskuläre Therapie eine größere Chance einer Gefäßeröffnung.
Patienten und Methoden: retrospektive Analyse von 33 Patienten mit Karotis-T-Gabelverschluss, bei denen eine mechanische Thrombektomie mit oder ohne Kombination einer i. v. Lyse durchgeführt wurde; das Patientenkollektiv wurde in Bezug auf Rekanalisation (TICI Scoring), funktionelles Outcome (NIHSS, mRS und Barthel-Index) und Mortalität verglichen.
Ergebnisse: Die mechanische Thrombektomie bei T-Gabel-Verschluss war in 82 % der Fälle erfolgreich (TICI 2b–3). Die Mortalität betrug 27 %. 3 Monate nach dem Ereignis konnte bei 64 % aller Patienten ein NIHSS-Shift von ≥ 4 und bei 49 % ein sehr guter mRS (0–2) bei einem Ausgangswert von 5 erreicht werden. Der Barthel-Index betrug nach 3 Monaten im Median 80.
Zusammenfassung: In diesem begrenzten Patientenkollektiv waren nach endovaskulärer Therapie das funktionelle Outcome besser und die Mortalität geringer als in der Thrombolyse-Literatur beschrieben (Rekanalisation: 20 %, Mortalität: bis 80 %, mRS 0–3: 21 %). Als ursächlich für diese überraschend guten Outcome-Daten wird die deutlich überlegene Rekanalisationspotenz der mechanischen Thrombektomie erachtet.

A 84 Gender aspects of acute stroke care: results from the Austrian Stroke Unit Registry

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Background: Gender related differences in quality of acute stroke care are an important concern with limited data available, specifically regarding the stroke unit setting. We used the prospective nationwide Austrian stroke unit registry to address this issue.
Methods: Our analysis covered the time period between January 2005 and December 2012 during which all patients with transient ischemic attack (TIA) or ischemic stroke, admitted to one of 35 Austrian stroke units, had been captured in the registry. These data were analyzed for age-adjusted preclinical and clinical characteristics and quality of acute stroke care in men and women. In addition, we assessed the outcome at three months in multivariate analysis.

Results: Over the 8-year study period 47209 individuals (47 % female) had received stroke unit care. Women were significantly older (median age: 77.9 vs. 70.3 years), had higher preexisting disability and more severe strokes. Correcting for age, no significant differences in quality of care parameters between males and females were identified with comparable onset-to-door times, times to and rates of neuroimaging and neurosonographic evaluations, as well as door-to-needle times and rates of intravenous thrombolysis (14.5 % for both genders). Despite equal acute stroke care and a comparable rate of neurorehabilitation, women retained a worse functional outcome at 3-months follow-up (modified Rankin scale score 3–5: OR 1.26 [95 % CI 1.17–1.36]), but a lower mortality (OR 0.70 [95 % CI 0.78–0.88]) after correcting for confounding variables.
Conclusions: We identified no significant differences in quality of care in the acute stroke unit setting between males and females. Further studies on the post-stroke period including socio-economic aspects are needed to clarify why female stroke patients have a diverging prognosis.

A 85

Myocardial infarction as a complication in acute stroke: results from the Austrian Stroke Unit Registry

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Background: Patients with transient ischemic attack (TIA) and stroke have an increased risk for subsequent cardiac events including myocardial infarction (MI), which might be associated with a worse clinical outcome. Rapid identification of stroke patients at higher risk for MI might foster intensified cardiac monitoring or certain therapeutic strategies.
However, information regarding acute MI as a complication of stroke in the very acute phase is limited. Moreover, there are no systematic data on the occurrence of MI following intracerebral hematoma. Thus, we aimed to assess the frequency, clinical characteristics, and short-term outcome of patients suffering from acute MI in the stroke unit setting.
Methods: We analyzed 46.603 patients from 32 Austrian stroke units enrolled in the prospective Austrian Stroke Unit Registry because of TIA/acute stroke over a 6-year period (January 1, 2007 to January 13, 2013). 41.619 patients (89.3 %) had been treated for TIA/ischemic stroke and 4.984 (10.7 %) for primary intracerebral hemorrhage (ICH). Acute MI was defined according to clinical evaluation, ECG findings and laboratory assessments. Patients with evidence for MI preceding the cerebrovascular event were not considered.
Results: 421 (1 %) patients with TIA/ischemic stroke and 17 (0.3 %) patients with ICH suffered a MI during stroke unit treatment for a median duration of 3 days. Patients with TIA/ischemic stroke and MI were significantly older, clinically more severely affected and had more frequently vascular risk factors, atrial fibrillation and previous MI. Total anterior circulation and left hemispheric stroke syndromes were more often observed in MI patients. Patients with MI not only suffered from worse short-term outcome including a higher mortality (14.5 % vs. 2 %; p<0.001) at stroke unit discharge, but also acquired more stroke complications like progressive stroke and pneumonia. Multivariate analyses identified previous MI and stroke severity at admission (according to the National Institutes of Health and Stroke Scale score) as factors independently associated with the occurrence of MI on the stroke unit.
Conclusions: While quite rare in the acute phase after stroke, MI is associated with a poor short-term outcome including a higher mortality. Patients with previous MI and severe stroke syndromes appear to be at particular risk for MI as an early complication in the stroke unit setting. Further studies are needed to determine whether increased vigilance and prolonged (cardiac) monitoring or certain therapeutic approaches could improve the outcome in these high-risk patients.

A 86

Systemische Thrombolyse bei Patienten mit Schlaganfällen der hinteren Zirkulation: Ergebnisse des österreichischen Schlaganfallregisters

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Hintergrund: Obwohl die systemische intravenöse Thrombolyse mit rt-PA für Patienten mit ischämischen Schlaganfällen der hinteren Zirkulation („posterior circulation stroke" – PCS) zugelassen ist, ist die Datenlage diesbezüglich mangelhaft. Studien betreffend rt-PA-Therapie, die zum Teil auch zur Zulassung führten, konzentrierten sich vor allem auf Patienten mit ischämischen Schlaganfällen der vorderen Zirkulation oder schlossen Patienten mit PCS sogar aus.
Wir untersuchten in einer großen Patientenkohorte, ob eine Therapie mit rt-PA das Outcome von Patienten mit PCS verbessert.
Methodik: Zwischen 2003 und 2013 wurden insgesamt 68.695 Patienten mit ischämischem Schlaganfall in das österreichische Schlaganfallregister eingeschlossen. Davon wurden insgesamt 1.188 Patienten mit PCS (594 Paare: mit rt-PA- und ohne rt-PA-Therapie) hinsichtlich Alter, Geschlecht, modified Rankin-scale (mRS) vor der Aufnahme, NIHSS bei Aufnahme, bekannter arteriellen Hypertonie, bekanntem Diabetes mellitus, bekannter Hyperlipidämie und Ätiologie (entsprechend der TOAST-Klassifikation) gematcht.
PCS wurde nach den Bamford-Kriterien definiert. Das Outcome wurde zum Zeitpunkt der Entlassung von der Stroke Unit mittels mRS gemessen. Zum Vergleich der Paare wurde der Wilcoxon-Test für gepaarte Stichproben verwendet.
Ergebnisse: Das mediane Alter der Paare war 70 (IQR 59–78) Jahre, 724 (61 %) waren männlich und die mediane NIHSS bei Aufnahme betrug 5 (IQR 4–8). rt-PA-behandelte Patienten hatte ein signifikant besseres Outcome (mRS: 2, IQR 1–4) als Patienten, die keine rt-PA-Therapie (mRS: 3, IQR 1–4) erhielten (p = 0,004). Komplikationen waren in beiden Gruppen selten, wobei symptomatische intrakranielle Blutungen bei Patienten mit rt-PA-Therapie etwas häufiger zu beobachten waren (1,5 % versus 0,2 %).
Diskussion: In unserer Studie konnten wir einen Nutzen der rt-PA bei Patienten mit PCS beobachten. Unsere Ergebnisse stützen die derzeitigen Therapieleitlinien, jedoch sind weitere Studien, die das funktionelle Outcome von Patienten mit PCS nach drei Monaten untersuchen, notwendig.

A 87

Acute spinal cord ischemia: critical analysis of delays for hospital admission and spinal cord imaging

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Background: Spinal cord infarction is a rare disease which varies in its pathogenesis, presentation, and outcome. A few case series have reported the successful utilization of reperfusion therapy including systemic thrombolysis and/or mechanical thrombectomy. Prompt recognition with subsequent neurological examination and adequate neuroimaging, however, are crucial for the implementation of treatment protocols aimed at restoring perfusion.

Aims: We sought to determine the time from symptom onset to admission to our Emergency Department (ED) and till spinal cord MR-imaging.

Material/Methods: We retrospectively analyzed patients diagnosed with acute spinal cord ischemia from 2011–2013. Subgroup analysis was performed for time to ED admission (<6 h, 6–24 h, and >24 h from symptom onset) and spinal cord MR-imaging (<1 h, 1–3 h, and >3 h).

Results: We identified 19 patients; mean age was 69 years (range 41–90 y). The median time from symptom onset to ED admission was 24 h (range 108 min – 3 months). In detail, 21 % were examined within 6 h, 37 % within 6–24 h and 42 % beyond 24 h. The pattern of presenting symptoms of patients with delayed admission did not differ from patients admitted earlier. Spinal cord MRI was performed after a median of 222 min (range 49 min – 5 days). MR-imaging was started within 1 hour in 11 %, between 1 and 3 hours in 37 % and >3 h in 53 % from admission. Subgroup analysis did not reveal a specific clinical impairment leading to earlier neuroimaging. The first MRI revealed T2-weighted hyperintensities in 78 %, on average the lesion stretched over 3.8 vertebral segments.

Conclusion: The window for treatment of ischemic stroke is narrow and minimization of the time from symptom onset to potential interventions is vital. A substantial proportion of our patients with acute spinal cord infarction, however, do not arrive at the ED in a suitable time for eligibility of reperfusion therapy. In contrast, adequate neuroimaging is performed relatively prompt, reflecting the contemporary management of patients with suspected stroke. Further knowledge of spinal cord infarction should be promoted in the general public and among medical professionals. In addition, it is compulsory to develop comprehensive treatment protocols to improve the often devastating outcome.

A 88 The Second European Carotid Surgery Trial (ECST-2)

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Background: Randomised trials have established the benefit of revascularisation by carotid endarterectomy(CEA) for moderate and severe carotid stenosis. However, a risk model derived from one of these trials and validated in another, showed that only patients with a high risk of stroke under medical therapy benefited from CEA. For a large range of patients there was neither clear benefit nor harm from CEA.

Medical therapy for stroke prevention has improved since these original trials, with more widespread use of statins, more active lowering of blood pressure and more effective antiplatelet regimes. Lower optimum targets have been set for risk factor control e.g. blood pressure. Therefore CEA may not be beneficial in many patients with carotid stenosis treated by modern optimized medical therapy (OMT).

Hypothesis: We hypothesize that in patients with carotid stenosis at low and intermediate risk for stroke, OMT alone is as effective in the long-term prevention of cerebral infarction and myocardial infarction (MI) as revascularisation and OMT combined.

Study design: ECST-2 is a multicentre, randomised, controlled, open, prospective clinical trial with blinded outcome assessment. We will use a risk model based on clinical characteristics to calculate a 5-year Carotid Artery Risk (mCAR) score, which will stratify patients as at high risk (≥15 %), intermediate risk (7.5–15 %), or low risk (<7.5 %) of future stroke using predictive data from previous trials recalibrated to take account of the likely benefit of OMT. An interim analysis using MRI to determine the 2-year rates of cerebral infarction and haemorrhage after randomisation will be performed to assess safety and feasibility of the design and inform the design and sample size calculations for the full trial. ECST-2 will incorporate baseline imaging of carotid plaque where possible to investigate the predictive value of plaque characteristics.

Centre requirements: A neurologist or physician with an interest in stroke; a surgeon with expertise in CEA; if available, an interventionist with expertise in CAS. Access to MRI.

Inclusion criteria: Patients with symptomatic or asymptomatic atherosclerotic carotid artery stenosis (>50 %, NASCET criteria), suitable for revascularisation with CAR score indicating low or intermediate risk.

Main exclusion criteria: Patients with a CAR score indicating high risk, patients refusing either treatment, unable to consent or unsuitable for revascularisation due to anatomy, ill-health or disabling stroke (current Rankin >2). Recent contralateral carotid revascularisation, cardiac or other major surgery.

Randomisation and treatments: Patients will be randomly allocated in equal proportions to be treated by 1) immediate carotid revascularisation with OMT or 2) OMT alone (in the latter arm, revascularisation may be performed at a later stage if it becomes more clearly indicated e.g. because of TIA during follow-up). Randomisation will be stratified by centre, type of planned revascularisation, symptom status and CAR score. A web-based randomisation system will be used. We anticipate that revascularisation will be by CEA in most patients, but carotid stenting (CAS) may be used if considered more appropriate. Centres will prespecify whether a patient will receive CEA or CAS if allocated to revascularisation. Randomisation and analysis will be stratified by the pre-specified intervention. The randomisation form will include entry of data to confirm a CAR score of <15 %. OMT in both arms will consist of all three of: 1) optimal antiplatelet therapy; 2) statin or other cholesterol lowering treatment with target total cholesterol of <4 mmol/l and LDL cholesterol of <2 mmol/L; 3) antihypertensive treatment, if required, with target blood pressure of 135/85 mmHg. Patients will also undergo risk factor modification e.g. advice on smoking.

Follow-up: The planned duration of follow up is a minimum of 5 years up to a maximum of 10 years. Recruitment and follow-up will be supervised by the neurologist or stroke physician. Follow-up will include ECG and troponin at 48 hours after revascularisation, with MRI at baseline and at 2 and 5 years follow-up.

Sample size: The planned sample size is 320 patients for the safety MRI analysis and 2000 patients for the full trial.

Primary outcome measures: For the full trial: any stroke at any time, plus non-stroke death occurring within 30 days of revascularisation. For the safety MRI analysis: The combined 2-year rate of cerebral infarction, cerebral haemorrhage, MI or periprocedural death after randomisation as assessed by follow up MRI and screening for MI.

Secondary outcome measures: Ipsilateral stroke, myocardial infarction, transient ischaemic attack or any hospitalisation for vascular disease during follow-up. Disabling stroke during follow-up. New cerebral infarction or haemorrhage on post procedural MRI. Ipsilateral restenosis or stenosis progression. Cognitive impairment. Further treatment procedure. Adverse events attributed to medical treatment or CEA. Quality of life and economic measures.

A 89 Ist Stammganglienblutung gleich Stammganglienblutung? Versuch der Subgruppenklassifizierung im Hinblick auf die Prognose

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Einleitung: Stammganglienblutungen sind eine häufige und mit erheblicher Morbidität und Mortalität einhergehende Erkrankung. Bisher fehlt in der Literatur eine durchgehende Subtypenbeschreibung der Stammganglienblutungen im Hinblick auf Pathogenese und vor allem Prognose. Welche Patienten von einer neurochirurgischen Operation und intensivmedizinischen Behandlung profitieren ist nicht geklärt.
Methode: Patienten mit Stammganglienblutungen der letzten 10 Jahre, die an der Universitätsklinik für Neurochirurgie stationär behandelt wurden, sind in diese retrospektive Analyse eingeschlossen worden. Sie wurden retrospektiv auf radiologische und klinisch-prognostische Parameter untersucht und das klinische Outcome der verschiedenen Subtypen wurde verglichen. Ausschlusskriterien waren der Blutung zugrunde liegende Tumoren oder Gefäßmissbildungen sowie intrakranielle Blutungen in anderen Lokalisationen oder aufgrund von Traumata. Eine Klassifizierung und Typisierung der Stammganglienblutungen nach neuroradiologischen Aspekten der funktionellen Anatomie und Topografie wird versucht.
Ergebnisse: Von 2004 bis 2014 wurden an der Salzburger Universitätsklinik für Neurochirurgie 158 Patienten mit Stammganglienblutungen behandelt. Das durchschnittliche Alter betrug 62 Jahre, das durchschnittliche Blutungsvolumen betrug 38 ml, 52 (32 %) Patienten verstarben innerhalb von 6 Monaten, 24 Patienten zeigten ein gutes Outcome (GOS 4 + 5). Bei 60 Patienten mit durchschnittlichen Volumina von 118 ml wurde die Blutung entleert. 120 Patienten (76 %) präsentierten sich zusätzlich mit Einblutungen in mindestens einen Seitenventrikel, hiervon wurde der größere Teil mit einer externen Ventrikeldrainage versorgt, ein kleinerer Teil erhielt intrathekal rekombinanten Thromboplasmin-Aktivator (rTPA) zur Fazilitierung der Blutdrainage. Prognostisch positivste Faktoren waren das jüngere Alter, ein hoher Präsentations-GCS, die Blutungslokalisation im Putamen sowie eine geringe Mittellinienverlagerung. Schlechteste Prognose hatten ältere Patienten mit totalen Stammganglienhämatomen und Einbeziehung der Pyramidenbahn und/oder des Thalamus.
Konklusion: Stammganglienblutungen bleiben vor allem aufgrund der primären Gewebsschädigung auch im 21. Jahrhundert oft mit schwerwiegenden neurologischen Ausfällen einhergehende und ebenfalls oft tödliche Erkrankungen. Bei günstigerer Lage und Blutungsmenge über 30 ml zeigte sich mit einer neurochirurgischen Hämatomentleerung im Vergleich zu den nichtoperierten Patienten öfters ein gutes Outcome, allerdings betreffen diese Kriterien eine kleinere Anzahl an Patienten. Besonders junge Patienten mit viel Mittellinienverlagerung und putaminalem Blutungstyp profitierten von einer neurochirurgischen Intervention. Bei Ventrikeleinbruch zeigte die intrathekale Anwendung von rTPA positive Ergebnisse.

A 90

Die transnasala Videoendoskopie des Schluckens als Feedback-Methode in der Therapie der neurogenen Dysphagie

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Sowohl Insulte als auch neurodegenerative Erkrankungen führen häufig zu Dysphagien. Die Krankheitseinsicht der Betroffenen ist allerdings oft eingeschränkt und notwendige Kompensationsmanöver werden nicht selbstständig im Alltag übernommen. Ein Grund dafür dürfte auch darin bestehen, dass auch schon für Gesunde der Schluckakt selbst nur wenig bewusst wahrgenommen wird, dies unter anderem auch, weil er ohne visuelles Feedback abläuft. Die transnasale Videoendoskopie des Schluckvorganges könnte eine Methode sein, den Patienten eben dieses visuelle Feedback zu bieten.

Die vorliegende Studie sollte als Grundlage für die weitere Erforschung der Fragestellung dienen, inwiefern die Videoendoskopie des Schluckens bei Personen mit neurogener Dysphagie als visuelle Feedback-Methode zur Verbesserung des Einsatzes von Kompensationsmethoden und zu einer größeren Steigerung der Kostformstufe führt.

Es wurde eine offene, randomisiert kontrollierte Studie mit 8 Probanden mit neurogener Dysphagie in zwei parallel laufenden Gruppen durchgeführt. Die Probanden der Feedback-Gruppe konnten die aus diagnostischen Gründen durchgeführte Videoendoskopie direkt mitverfolgen. Die dabei gewonnenen Videoaufnahmen wurden in der logopädischen Therapie systematisch als Therapiematerial eingesetzt und dem Patienten wiederholt vorgespielt. Die Kontrollgruppe erhielt diese zusätzliche Information nicht.

Im Rahmen der Pilotstudie sollten die Rekrutierungsrate, die Durchführbarkeit des Studienprotokolls und die Eignung der Messinstrumente eruiert werden. Zusätzlich sollten erste Hinweise gewonnen werden, ob es zu einer Verbesserung in der selbstständigen Anwendung von Kompensationsmethoden kommt und Unterschiede im Bogenhausener Dysphagie-Score (BODS-2) und im Swal-Care, einem Maß für die Versorgungsqualität und Zufriedenheit von Dysphagiepatienten, zu erreichen sind.

Das Studienprotokoll erwies sich als sehr praktikabel, die Probanden nahmen die Intervention gut an, es gab keine Drop-outs. Beide Gruppen verbesserten sich in der Anwendung von Kompensationsmanövern, die Feedback-Gruppe steigerte sich stärker. Bei den bislang kleinen Fallzahlen wurde auf eine Berechnung der Signifikanz der Ergebnisse verzichtet.

Eine größer angelegte Studie zur Erforschung der Effektivität der Videoendoskopie als Feedback-Methode ist machbar. Aus diesen Gründen ist eine Fortführung der Studie im NRZ Rosenhügel geplant.

A 91 Nächtliches Blutdruckverhalten bei Schlaganfallpatienten mit Schlafapnoe – Einfluss von Ätiologie, Komorbidität, Medikation und zerebralem Stromgebiet

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Fragestellung: Schlaganfallpatienten mit SA zeigen im klinischen Alltag ein unterschiedliches Blutdruckverhalten auf respiratorische Ereignisse. Ziel der Studie war die Evaluierung der Einflussfaktoren Alter, Komorbidität, Klinik, Medikation, Ätiologie und zerebrales Stromgebiet auf das nächtliche systolische BD-Verhalten bei Schlaganfallpatienten mit Schlafapnoe (SA).

Patienten und Methoden: Im Rahmen der stationären neurologischen Rehabilitation wurde bei allen kardiorespiratorischen Polygrafien an Schlaganfallpatienten im Alter von 18 bis 70 Jahren der systolische Blutdruck mittels der Puls-Transit-Zeit-(PTZ-)Methode bestimmt (SOMNOmedics GmbH, Randersacker, Germany). Dabei wurden eine individuelle Ausgleichskorrektur und Synchronisierung der PTZ mit dem systolischen RR-BD durchgeführt. Die Anzahl der systolischen Anstiege > 15 mmHg pro Stunde wurden gescort. Neben der Erhebung der Risikofaktoren erfolgte eine ätiologische Klassifikation nach TOAST- und eine anatomische nach Oxfordshire-Community-Stroke-Project-(OCSP-)Kriterien.

Ergebnisse: Von 203 Schlaganfallpatienten (39 w, 164 m; 58 ± 12 Jahre; BMI: 29 ± 5) zeigten 38 % eine SA (AHI > 15) mit vorwiegend obstruktiven Apnoen (86 %). Dabei fanden sich durchschnittlich 47 ± 38 BD-Anstiege pro Stunde mit einem mittleren Anstieg von 19 ± 3 mmHg und ein durchschnittlicher nächtlicher systolischer BD von 138 ± 26 mmHg (bei 46,8 % > 140 mmHg). Bei 7 Patienten (5 m, 2 w) fanden sich keine adäquaten Blutdruckanstiege auf Apnoen (Non-Responder). Unter den Non-Respondern fand sich eine gleichmäßige ätiologische Verteilung auf Mikroangiopathie (3), Makroangiopathie (1), Blutung (1), andere Ursache (1), kardiale Embolie (1) und unklare Genese (1). Im OCSP-Stromgebiet fanden sich keine Unterschiede. Alter, Komorbidität und Medikation waren ebenfalls keine signifikanten Einflussfaktoren für die Gruppe der Non-Responder.

Schlussfolgerungen: 9,1 % der Schlaganfallpatienten mit SA zeigen ein untypisches Blutdruckverhalten nach Apnoen (Non-Responder). Es besteht jedoch kein Zusammenhang mit Alter, Komorbidität, Klinik, Medikation, Ätiologie und zerebralem Stromgebiet.

A 92 An exploratory study on the effect of mobility training in chronic stroke patients

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Stroke and age-related cerebral white matter hyperintensities (WMH) increasingly occur with advancing age. Both are associated with impaired mobility and cognition, but it is still unclear, whether the severity of pre-existing WMH influences outcome after mobility rehabilitation in stroke.

Thus, we set-up a study investigating chronic stroke patients with different severity of WMH and residual mobility impairment due to the stroke, using clinical, motor and cognitive assessments, and structural and

functional MRI (ankle movement) at 3 T, before and after training. 7 patients so far participated in 5 weeks of professionally guided mobility rehabilitation. A matched control group of 7 healthy elderly individuals was tested twice without intervention. Patients improved in the "de Morton Mobility Index" (pre=74; post=80) and regarding episodic memory function (pre=23; post=29) after 5 weeks of mobility training. On fMRI, patients of the training group demonstrated increased activation of the precuneus and lateral occipital region before the training, compared to follow-up. Further dedicated analyses of this ongoing study including a region-of-interest approach and regression analyses to identify functional correlates of performance gains in a larger sample will be presented at the congress.

A 93

Alterations of tryptophan metabolites in serum and cerebrospinal fluid in patients after stroke

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Background: Alterations of tryptophan metabolites have been described in several neurological diseases as Alzheimer's, Parkinson's, Chorea-Huntington or epilepsy. Aim of the present study was to investigate alterations of tryptophan metabolites in the serum and cerebrospinal fluid (CSF) of patients after stroke and compare with corresponding control subjects.
Methods: The amount of tryptophan and tryptophan metabolites L-kynurenine, kynurenic acid and anthranilic acid in serum and CSF of stroke patients (n=54) and control subjects (n=26) was analysed by high performance liquid chromatography. The stroke patients were divided in two groups: subacute infarction (n=23) and elder than 3 months infarction (n=16). Also a group of TIA/PRIND (n=15) patients was included in this investigation. Alterations of tryptophan metabolites and ratios between metabolites were investigated. Influence of sex, age and dimension of the infarction were evaluated. The statistical analysis was carried out by one-way-ANOVA and Student's T-Test. The study was performed according to the ethical regulations of the government of Lower Austria.
Results: After stroke tryptophan levels were significantly increased in the serum and in CSF compared with controls. This increase was more pronounced in female stroke patients and in the group elder than 50 years. The content of L-kynurenine and anthranilic acid increased too, but the effect was not statistically significant. Kynurenic acid levels were not altered in the serum but considerably lowered in CSF, especially in female stroke patients. The dimension of infarction did not influence significantly the alteration of tryptophan metabolites.
Discussion: Changes of tryptophan levels after stroke were found not only in the central nervous system but also in the periphery suggesting diminished tryptophan metabolism due to impaired tissue conditions induced by stroke. Reduction of kynurenic acid in the CSF after stroke could be related to the increased risk of epileptic events.
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A 94 Moyamoya disease associated with elliptocytosis leading to haemodynamic cerebral infarction – a case report

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Background: Moyamoya disease is characterised by progressive stenosis of the internal carotid arteries and their proximal branches. Hereditary spherocytosis is a common hematologic disorder characterized by hemolytic anemia and splenomegaly.
Case report: We report a 40-year-old male patient with known hereditary spherocytosis who presented with an acute left-sided hemiparesis, hypesthesia and aphasia in association with acute haemolytic crisis caused by gastrointestinal infection.
Brain magnetic resonance (MR) imaging revealed recent cerebral infarction in the territory of the right middle cerebral artery and global reduced perfusion in both hemispheres. The MR angiographic findings were compatible with the diagnosis of moyamoya disease.
During his stay the patient reported a worsening of the left-sided paresis and sensory symptoms as haemoglobin decreased below 7 mg/dl. Blood transfusion was needed to stabilise his clinical condition. An extra-intracranial anastomosis operation was carried out for treating moyamoya disease, concerning spherocytosis a splenectomy was done.
Conclusion: Anaemia is thought to exacerbate neurological outcome in stroke patients by reduced oxygen delivery, however, an increase in blood viscosity may also worsen hypoxia in post-stenotic brain regions. Cerebral oxygen delivery is known to be constant as it decreases to less than 10 g/dl by compensatory vasodilatation mediated by nitric oxide which may be beneficial in cerebral artery stenosis or collaterals. However, there is no convincing evidence to guide clinicians in deciding when to transfuse anemic stroke patients in general. In reduced cerebrovascular reserve as in our case of moyamoya disease hemoglobin levels lower than 7 g/dl may appear critical.

A 95 Akutbehandlung und Sekundärprophylaxe bei einem Antiphospholipid-Syndrom (APS) assoziierten M1-Verschluss – ein Fallbericht

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Hintergrund: Das Antiphospholipid-Syndrom (APS) ist durch eine erhöhte Thromboseneigung und/oder Aborte sowie dem Nachweis von AP-Antikörpern charakterisiert. Der ischämische Schlaganfall zählt zu den häufigsten Komplikationen, pathogenetisch werden kardioembolische und lokal-thrombotische Mechanismen unterschieden. Patienten mit einem APS-assoziierten Schlaganfall tragen ein erhöhtes Risiko für weitere ischämische Ereignisse, sodass der Sekundärprophylaxe eine besondere Bedeutung zukommt.
Fallbericht: Bei einer 48-jährigen Patientin mit einem im Rahmen des Akutgeschehens neu diagnostizierten APS kam es zu einer

plötzlichen Broca-betonten Aphasie mit leichtgradiger Hemiparese rechts (NIHSS 3). Die Diagnose eines Verschlusses im M1-Abschnitt der linken A. cerebri media (ACM) bei noch fehlender Diffusionsstörung wurde mittels MRT/MRA gestellt. Es bestand eine absolute Kontraindikation für eine systemische Lysetherapie (Thromboztopenie 67,00 g/l), sodass 2 Stunden und 30 Minuten nach Symptombeginn eine Angiografie zur mechanischen Rekanalisation begonnen wurde.

Nach zunächst erfolgreicher Thrombektomie traten wiederholt Reokklusionen auf, sodass eine Stentimplantation erfolgte.

Am darauffolgenden Tag zeigte sich in der transkraniellen Duplexsonografie (TCD) eine hochgradige Stenose im distalen Stentbereich (V_{max} 300 cm/s).

Am ersten postinterventionellen Tag wurde mit einer Sekundärprophylaxe bestehend aus doppelter Plättchenaggregationshemmung begonnen.

Fünf Tage nach Intervention kam es zum akuten Auftreten eines schweren linksseitigen Media-Syndroms (NIHSS 9). In der akut durchgeführten MRT demarkierte sich ein neues diffusionsgestörtes Areal im Stromgebiet der linken ACM, MR-angiografisch konnte kein sicherer Kontrastmittelfluss dargestellt werden. Von einer erneuten Angiografie wurde unter Berücksichtigung eines erhöhten Einblutungsrisikos abgesehen. Drei Monate nach dem Erstereignis zeigte die Duplexkontrolle eine komplette Rekanalisation der In-Stent-Thrombose, sodass eine Umstellung der Sekundärprophylaxe auf Azetylsalizylsäure und Phenprocoumon erfolgte. Die neurologische Residualsymptomatik bestand aus einer diskreten Parese der oberen Extremität rechts sowie einer diskreten Broca-betonten Aphasie (NIHSS 2).

Diskussion: Bislang waren in der Literatur zwei Fälle einer erfolgreichen intraarteriellen Thrombolyse beim APS-assoziierten M1-Verschluss bekannt. Unser Fallbericht zeigt die Möglichkeit einer mechanischen Rekanalisation mit zusätzlicher Stentimplantation aufgrund der Gefahr einer Reokklusion auf. Der Fall legt allerdings nahe, dass auch postinterventionell von einem erhöhten Risiko für eine In-Stent-Thrombose auszugehen ist. Es muss daher diskutiert werden, ob bereits in der Akutphase eine effektivere medikamentöse Prophylaxe forciert werden sollte.

A 96

Symptomatic bleeding from an intracerebral cavernoma after intravenous thrombolysis for ischemic stroke

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Cerebral cavernous hemangiomas (CCH) are one of the most frequent vascular malformations in the brain and often just an incidental finding on neuroimaging. CCH bleeding risk is generally considered to be low and it is currently not recommended to search for CCH before the application of intravenous thrombolysis for acute ischemic stroke. There exists only one single report that has shown that thrombolysis was safe in a patient with an accompanying silent CCH.

We here report the case of a 58-year-old man, who presented with an acute onset of dysarthria, mild right-sided motor weakness and horizontal gaze palsy (National Institutes of Health Stroke Scale score, NIHSS, of 6). Acute brain computed tomography showed no morphologic changes except for a calcified 5-millimeter lesion in the frontoparietal white matter, which was suspicious for a cavernoma. Assuming an acute brainstem ischemia the patient subsequently received intravenous recombinant tissue plasminogen activator 2.5 hours after symptom onset and clinically improved to NIHSS of 4. Ten hours after thrombolysis, however, the patient suddenly deteriorated and developed a dense hemiparesis, predominantly affecting the leg. Brain MRI showed a 4.0 x 2.3 x 4.0 centimeter large frontoparietal ICH at the exact location of the previously suspected cavernoma.

Our observation suggests that systemic thrombolysis with rt-PA in the presence of a CCM might not always be harmless. In conclusion, further observational data are needed to allow for more informed risk-benefit stratification in stroke patients with incidental cavernomas that are considered for administration of thrombolytic agents.

Schmerz

A 97 Galanin-Plasmakonzentration in der akuten Migräneattacke

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Hintergrund: Die Migräne ist mit einer Prävalenz von über 10 % eine der häufigsten neurologischen Erkrankungen. Ihre Auswirkungen auf die Lebensqualität der Betroffenen, aber auch die volkswirtschaftlichen Kosten sind enorm. Die zugrunde liegenden pathophysiologischen Mechanismen sind noch nicht vollständig geklärt, eine zentrale Rolle spielt aber das trigeminovaskuläre System. Eine Aktivierung nozizeptiver Afferenzen führt zur Ausschüttung von Neuropeptiden wie Calcitonin Gene-Related Peptide und Substanz P, welche zur Vasodilatation und Proteinextravasation, aber auch zur Nozizeptorsensibilisierung führt. Ein Einfluss des Neuropeptids Galanin auf die Nozizeption ist tierexperimentell gesichert. Weiters gibt es Hinweise für eine Beteiligung von Galanin an der Cortical Spreading Depression, die für die Migräneaura verantwortlich gemacht wird. Ein direkter Zusammenhang zwischen Galanin und Migränekopfschmerzen beim Menschen ist bislang aber nicht untersucht.

Ziel: In diesem Projekt soll die Plasmagalaninkonzentration bei Migränepatienten mit und ohne Aura in der akuten Attacke und im schmerzfreien Intervall nach frühestens einer Woche untersucht und mit gesunden Kontrollpersonen verglichen werden.

Patienten und Methode: Es wurden bislang 8 Patienten (6 weiblich, 2 männlich; Alter 33,8 ± 11,7 Jahre) in der akuten Migräneattacke bzw. 6 Patienten im schmerzfreien Intervall sowie 8 gesunde Kontrollpersonen (3 weiblich, 5 männlich; Alter 36,3 ± 9,7 Jahre) untersucht. Bei 4 Patienten besteht eine Migräne mit und bei ebenfalls 4 eine Migräne ohne Aura. Die Konzentration von Galanin wurde aus EDTA-Blut mittels Radioimmun-Assay (RIA) bestimmt.

Ergebnisse: Nach Korrektur der Plasmagalaninkonzentrationen mit einem „nonspecific binding" lag der Mittelwert in der Migräneattacke bei 19,16 fmol/ml (± 4,27) und im beschwerdefreien Intervall bei 17,07 fmol/ml (± 3,13). Bei den Probanden lag der Wert bei 12,45 fmol/ml (± 5,05). Obwohl statistisch nicht signifikant (Studentscher t-Test, p = 0,26), sind die Werte im Vergleich zum schmerzfreien Intervall in der akuten Migräneattacke erhöht. Die Galaninkonzentrationen in der Migräneattacke sind hingegen im Vergleich zur Kontrollgruppe statistisch signifikant höher (p = 0,02). Zwei Patientinnen gaben eine sensible bzw. visuelle Aurasymptomatik an. Die Galaninkonzentrationen dieser beiden Patientinnen in der Migräneattacke differierten nicht signifikant (p = 0,06) im Vergleich mit den Migräneattacken ohne Aura.

Schlussfolgerung: Unsere bisherigen Ergebnisse zeigen, dass die Plasmagalaninkonzentrationen in der akuten Migräneattacke ausreichend hoch sind, um bestimmt werden zu können. Erhöhte Galaninkonzentrationen deuten auf eine wichtige Rolle dieses Neuropeptids in der Pathophysiologie der Migräne hin.

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