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001

Brain network for emotional body language reading: Structural and effective connectivity analysis

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Reading and understanding body language is indispensable for successful non-verbal communication and daily-life social interaction. Yet, despite this significant clinical impact, the underlying brain networks remain little understood and deficits after brain damage rarely considered and recognized. The aim of the study was to assess the architecture of the brain networks for body language reading, by developing a new analysis of functional and structural connectivity. To this end, we performed functional MRI (fMRI) and diffusion tensor imaging (DTI) during recognition of emotions (happy, neutral and angry) conveyed by a point-light arm seen knocking on a door. Statistical Parametric Mapping (SPM12; The Wellcome Trust Centre for Neuroimaging, London, UK, <http://www.fil.ion.ucl.ac.uk/spm>) was used for data pre-processing, fMRI data and dynamic causal modelling (DCM) analysis of effective connectivity were performed with SPM12, and the FMRIB Software Library (FSL4, Oxford Centre for Functional MRI of the Brain, UK, <http://www.fmrib.ox.ac.uk/fsl>) for probabilistic tractography on the DTI data. The results show that the right superior temporal sulcus (STS) and caudate nucleus are preferentially activated by happy, and the left inferior insula, perigenual anterior cingulate cortex (ACC) and posterior midcingulate cortex (MCC) by angry as compared to neutral body motion. The cerebellar vermis (lobule IX) and right amygdala appear to signal a lack of emotional content. Effective and structural connectivity analysis demonstrates functional architecture within this network. This study for the first time reveals the components, structural connections and functional interactions of the brain network for reading of emotional body language reading. The data contribute to better clinical consideration and understanding of socio-cognitive deficits after damage to this network. In addition, the developed effective-structural connectivity analysis may open new perspectives in task-related brain imaging assessment of different functional networks in normalcy and neuropsychiatric pathology, outside the immediate field.

002

Sensor-based recognition of activities of daily living as pre-marker for cognitive decline

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Background

Cognitive impairment due to dementia decreases functionality in Activities of Daily Living (ADL), leading to reduced autonomy and increased need for care. Its assessment is useful to determine the care needs, to identify risks in daily life and to monitor disease progression or effects of anti-dementia treatments. In this study, we use a wireless unobtrusive sensor network that can recognise individual ADL and we investigate differences in ADL pattern and performance between dementia patients and healthy controls.

Methods

A wireless unobtrusive sensor network was set up in the homes of ten independently living dementia patients (6 women, 4 men; mean age = 73.9 years; SD = 6.7 years; age range 63-87 years) and ten age- and gender-matched healthy controls (6 women, 4 men; mean age = 76.7 years; SD = 8.2 years; age range 64-94 years). Around 9,600 person-hours of continuous activity data were collected during a period of 20 days. The data were analysed and categorized using a machine learning (in-house developed) classification algorithm to detect individual ADL. Thereafter, ADL activity maps were setup to compare the behavioral patterns of healthy controls and dementia patients. The heterogeneity of the recognised ADL was calculated and its accuracy to discriminate patients from healthy controls was analysed.

Results

The behavioral patterns of the two groups exhibit significant differences, particularly in regularity of patterns and in overall daily structure which is depicted in the activity maps. Activity maps of dementia patients reveal unorganised behaviour patterns. ADL heterogeneity differed significantly between the study groups. The discriminating accuracy increases with observation duration and reaches 0.95 for 20 observation days.

Interpretation

The wireless sensor system is able to identify data patterns and assign these to eight specific ADL. Owing to its discrete approach, the system maintains a high level of participant privacy. These unobtrusive sensors seamlessly integrate into the home of test subjects and can quantify ADL relevant behaviour. They are a useful tool to uncover the relationship between cognitive impairment on ADL, to quantify ADL-relevant changes in the course of a patient's dementia and to measure additional functional outcomes of anti-dementia treatments.

003

Ischemic stroke in women using contraceptives: causes, characteristics and outcome

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Background

Oral contraceptive usage may increase stroke risk in young women. We aimed at assessing characteristics and outcome of acute ischemic stroke (AIS) in women below age of 50 while on oral contraceptives.

Methods

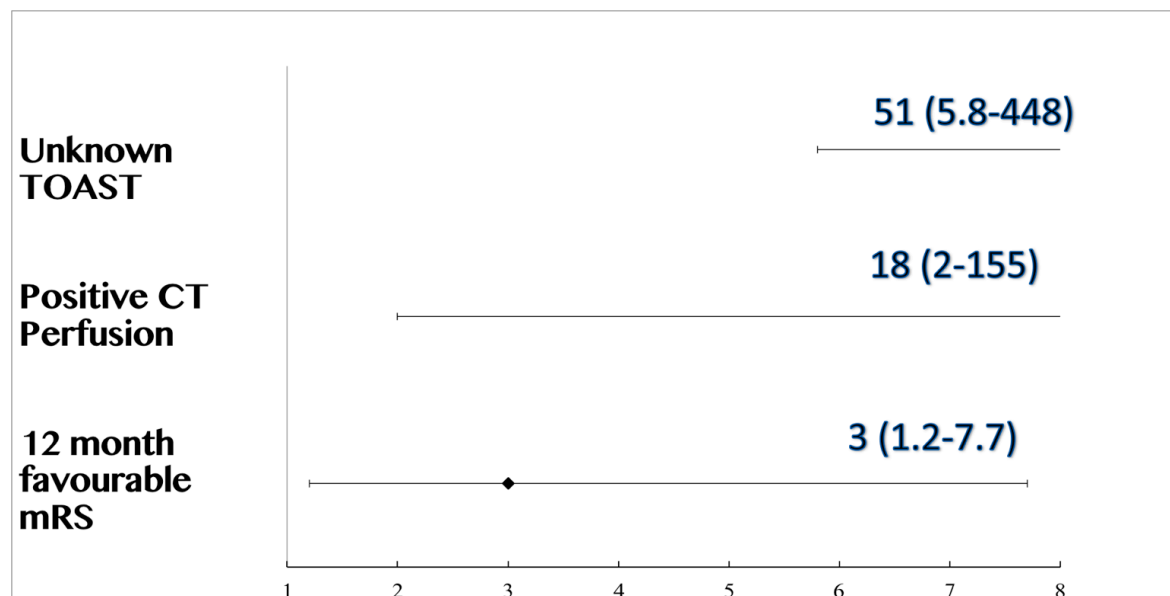
We used consecutive AIS between 2003 and 2015 from the ASTRAL registry with detailed determined demographics, risk factors, clinical, radiological and prognostic data. We compared female patients <50 years with and without contraceptive usage in a multiple logistic regression model, with contraceptive use as the dependent variable.

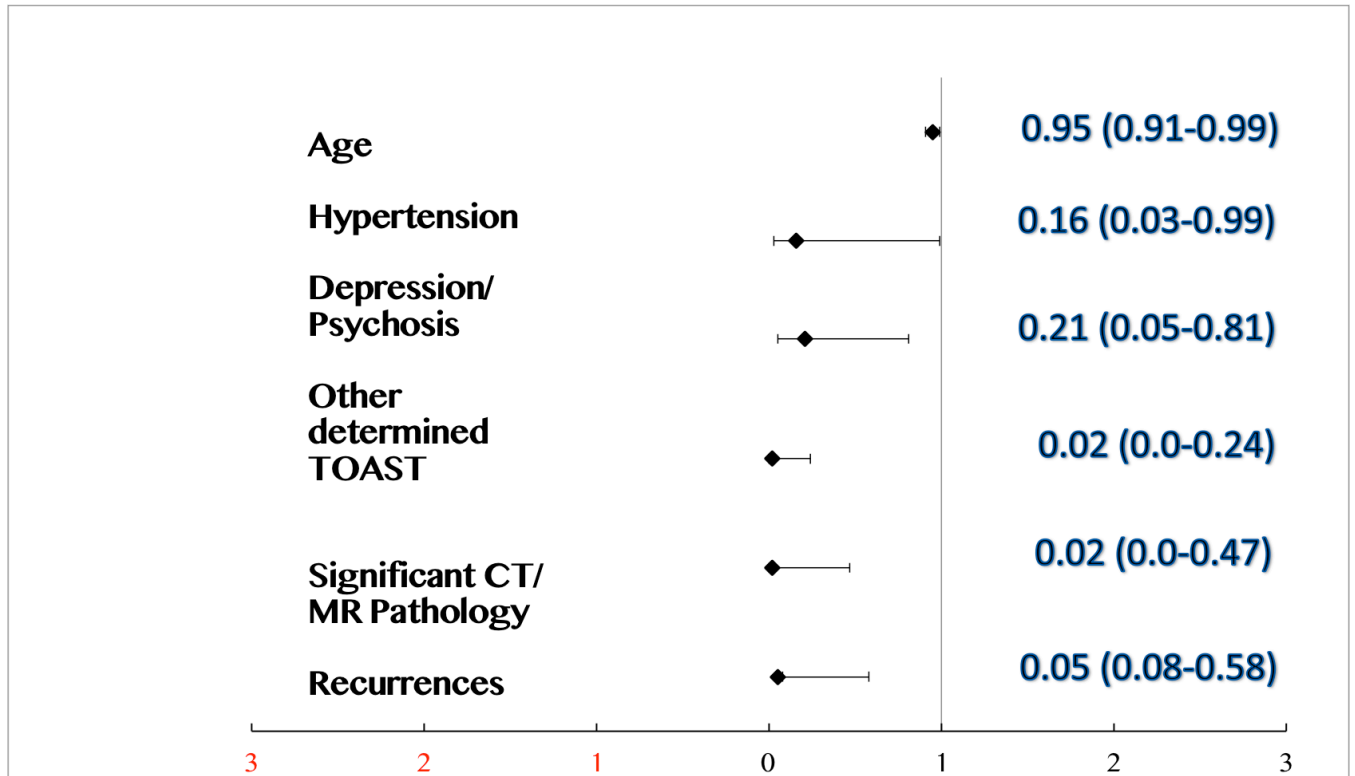
Results

Of the young 179 women identified, 57 used contraceptives: oestrogen and progesterone (n=43), progesterone only (n=10), and unknown (n=4). Stroke in contraceptive users occurred at a significantly younger age and in women with significantly lower history of hypertension or previous psychosis or depression. Initial stroke severity was similar, but a significantly higher proportion of contraceptive users had unknown stroke (TOAST) mechanism. PFO prevalence was similar, 17.54% in contraceptive users vs. 14.75% to non-users. These patients had significantly less intra and extracranial stenoses and occlusions and more often positive CT perfusion studies. Adjusted functional outcome was similar at 3 months and more favourable at 12 months in contraceptive users with significantly fewer stroke recurrences.

Conclusions

Women using contraceptives have strokes at a young age, with less arterial pathology, and less identified stroke mechanisms. Together with a lower recurrence rates after discontinuing contraceptives, an important causative role of contraceptives in stroke is suggested. The stroke mechanism being often unexplained, a prothrombotic state or hitherto unrecognized mechanisms may be responsible.





004

Differences in processing proprioceptive input from the neck muscles may explain the benefit from sensory tricks in patients with idiopathic cervical dystonia

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Objective

We used a paradigm of neck vibration to test the hypothesis that the sensory trick (ST), which is used by some patients with idiopathic cervical dystonia (CD) to alleviate their dystonic posture, modulates the processing of proprioceptive information.

Background

Muscle vibration activates muscle spindles and can thus be used in the experimental setting as a proprioceptive stimulus simulating muscle lengthening. Applied over neck muscles during stance, vibration modulates global body orientation, which usually leads to a tonic forward sway in healthy persons. This postural response has been reported to be diminished or absent in CD patients.

Methods:

21 CD patients with a ST, 15 CD patients without ST and 16 healthy controls (HC) were recruited. Neck muscle vibration (100 Hz for 10 sec.) was applied bilaterally over the upper trapezius under three different conditions: 1) Quiet standing; 2) standing while performing the ST (or ST-like movement in the control groups); 3) standing while elevating the flexed arm without touching any part of the body (i.e. sham ST). Centre of pressure position and ankle, hip and neck angles in the sagittal plane were analysed.

Results

For HC in all three conditions, neck muscle vibration led to an initial forward sway of the body that slowly increased during the prolonged vibration. CD patients with a ST showed a similar pattern of sagittal sway. However, in patients without a ST, the initial sagittal sway was significantly reduced in all three conditions ($p < 0.001$) and the later slow increase was absent ($p = 0.024$). In general, the response was mediated by an ankle flexion in combination with a simultaneous hip extension and a tendency to extend the neck. Ankle flexion and neck extension were reduced in patients without a ST, whereas hip extension was significantly reduced in those with a ST. However, contrary to our hypothesis, the ST did not have an effect that was specific to either or both CD groups for any aspect of the postural response.

Conclusions

Our results suggest that processing of proprioceptive input from the neck muscles in CD patients with an effective ST is similar to HC, while patients without any ST are far less sensitive to this input. This difference in sensitivity to proprioceptive input for postural control could be an important trait that determines if CD patients benefit from ST or not.

005

Mitochondrial cytopathy with common MELAS mutation presenting as multiple system atrophy mimic

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Introduction

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome is one of the most frequently inherited mitochondrial disorders. It is a multi-organ disease with broad manifestations. We describe a patient with a partial clinical manifestation of MELAS syndrome harboring the most common m.3243A>G mutation in the MT-TL1 gene, who additionally presented with a multisystem atrophy phenotype with cerebellar predominance.

Case

In 2012, a 60-year-old male was referred for progressive gait abnormalities. He reported deteriorating unsteady gait and fatigue of the lower extremities. Personal history revealed diabetes, sensorineural hearing loss, and fatigue. Family history was remarkable for tetraparesis of unknown origin in his mother. Examination revealed cerebellar dysarthria, left-sided hyperreflexia, atrophic proximal tetraparesis, slight ataxia of the left upper limb and distally reduced vibration sense of the lower extremities with positive Romberg's test. The combination of atrophic paresis, diabetes, sensorineural hearing loss, signs of multisystemic affection of the central nervous system and potential maternal inheritance led to the clinical suspicion of mitochondrial cytopathy. Biopsy of the left deltoid muscle displayed findings compatible with mitochondrial myopathy. Magnetic resonance imaging showed bilateral calcifications of the basal ganglia, thalami, nuclei dentate, pons and infratentorial atrophy. Sequencing revealed the common MELAS mutation m.3243A>G in the MT-TL1 gene. After three years of clinical stability, he presented with deterioration of gait. Examination revealed disease progression with a marked cerebellar, pyramidal and an extrapyramidal syndrome. Gait was ataxic with a spastic component. FDG-PET of the brain supported the suspicion of multiple system atrophy (MSA) with cerebellar predominance. Diagnosis of MSA mimic due to mitochondrial cytopathy was made and the patient was started on levodopa with improvement in walking and faster turns.

Discussion/Conclusion

To our knowledge this is the first patient with the common mutation associated with MELAS who presents with a multiple system atrophy mimic. This observation widens the spectrum of phenotypes associated with mitochondrial cytopathies in general, and with MELAS in particular. Mitochondrial cytopathy should be included as differential diagnosis in patients with a MSA-C phenotype and (family) history suggestive of mitochondriopathy.

006

Short- and long-term outcome of microscopic lumbar spine surgery in patients suffering from predominant back or predominant leg pain

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Background

Traditionally, spine surgeons are hesitant to operate on patients with predominant axial low back pain (LBP) and subordinate irradiating leg/buttock pain. The aim of this study was to assess, whether predominant back pain (pBP) represents a negative outcome predictor in patients undergoing microscopic spine surgery without fusion for a lumbar disc herniation (LDH) or spinal stenosis (LSS).

Methods

Retrospective analysis of prospectively collected data on consecutively recruited patients with LDH or LSS scheduled for spine surgery at two Swiss teaching hospitals. Patients with Visual Analogue Scale (VAS) back pain equal or greater than VAS leg pain before surgery were assigned to the pBP group, and compared with patients with predominant VAS leg pain (pLP). Outcome measures included the Roland-Morris disability index (RMDI), Oswestry disability index (ODI), as well as the health-related quality of life (hrQoL) measures Short Form (SF)-12 physical component summary (PCS) and EuroQol (EQ-5D) index, at three days (D3), six weeks (W6), six months (M6) and one year postoperative (Y1). The W6-responder status of patients of the pBP group on each of the scales was analyzed.

Results

A total of n=325 patients, n=154 (47.4%) with pBP and n=171 (52.6%) with pLP, were included. There was no significant difference between the group means of the RMDI, ODI, SF-12 PCS or EQ-5D at any time point from D3 over W6, M6 until Y1. Most improvement on the RMDI, ODI, SF-12 PCS and EQ-5D was observed until the W6 follow-up with little or no improvement thereafter up to Y1. Patients with pBP were as likely as patients with pLP to be W6-responders on the RMDI (OR 0.90, 95%CI 0.38–2.13, p=0.810), ODI (OR 1.05, 95%CI 0.54–2.04, p=0.877), SF-12 PCS (OR 1.18, 95%CI 0.63–2.22, p=0.613) and EQ-5D (OR 0.62, 95%CI 0.32–1.19, p=0.151).

Conclusions

The present data suggest that patients with pBP have a comparable functional and hrQoL outcome at W6 after surgery for LDH or LSS to patients with pLP. Also, up to one year postoperative, no differences on the generic or disease-specific metrics were found between pBP and pLP patients. There appears to be no reason to preclude patients with LDH or LSS and predominant back pain but otherwise concordant clinico-radiological findings from surgical therapy.

007

Diagnostic under-grading in IDH wildtype gliomas due to small pathological tissue samples

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Purpose

Neurosurgeon's generosity for tissue sampling during glioma resections is thought to vary significantly. In contrast to IDH mutation analysis, which is homogenous within a given tumor, diagnostic errors in histological analysis following the standard guidelines of WHO grades (WHO°) could be due of small tissue samples as a result of histological heterogeneity. In this study we want to assess whether the size of the tissue sample sent to histopathology influences the tumor grading in IDH wildtype (IDH-wt) gliomas.

Methods

Demographics, histological diagnosed WHO°, tissue sample volume and pre-operative MRI tumor volume Data of 116 patients aged 18 to 88 who received a resection of a IDH-wt gliomas between January 2007 and December 2015 at the Department of Neurosurgery at the University Hospital in Bern were evaluated. The differences between absolute and relative pathological sample sizes stratified by WHO° were conducted using Mann-Whitney U Test and One-Way Permutation Test. Survival analysis was performed using Kaplan-Meier method with Long-Rank Test.

Results

With a mean tissue sample size of 10.7 cc (0.02-92.9) 97 patients (83.6%; mean age 60.2 years) were histologically diagnosed as WHO° IV, while 19 patients (16.4%; mean age 53.7 years) with a mean tissue sample size of 2.52 cc (0.1-9.0) were diagnosed as WHO° III/II (15 WHO° III, 4 WHO° II). One Way Permutation Test showed a significant difference between absolute tissue samples stratified by WHO° ($p=0.0374$). The distribution of preoperative tumor volumes with WHO° IV vs. WHO° III/II showed no significant difference ($p=0.7825$). Of all 116 tumors with a sample size $>10\text{cc}$ 100% were pathologically diagnosed as WHO° IV and of all with sample size $>5\text{cc}$ 93.5% were diagnosed as WHO° IV. Further Survival analysis revealed that the survival of the WHO° II/III gliomas was significantly longer than of the WHO° IV gliomas ($p=0.016$). Mean overall survival of patients with WHO° II/III gliomas lived only 12.6 month longer than those with WHO° IV glioma.

Conclusion

Small tissue sample sizes are associated with a higher risk of under-estimating malignancy in histological grading in IDH-wt gliomas. This study suggests a standard minimum tissue sample size ($>5\text{cc}$) in every resection and supports the efforts in raising the relevance of molecular markers. Modalities of adjuvant treatment for IDH-wt WHO II°/III° gliomas need to reflect a prognosis that is only marginally better than that of a glioblastoma.

008

Act locally: the 3q26 genes SOX2, PIK3CA, MFN1 and OPA1 co-regulate GBM cell invasion

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Background

3q26, a major target for genetic alterations in GBM, contains the genes encoding transcription factor SOX2, growth-factor-AKT signaling activator PIK3CA, and two effectors of mitochondria fusion MFN1 and OPA1. Since mitochondria fission is a pre-requisite for cell motility, we aim at determining the roles of these four genes in GBM cell invasion.

Methods

Parental LN319 GBM cells and those knocked-down for 3q26 genes were tested for invasion, migration and proliferation parameters, mitochondria morphology, AKT pathway activation status, SOX2 subcellular location and 3q26 gene promoter activation.

Results

All four knock-downs consistently enhanced cell invasion and motility, reduced proliferation, and shortened mitochondria. This common phenotype suggested that the four 3q26 genes act on the same pathway. Ongoing chromatin immuno-precipitation and luciferase reporter gene assays show that SOX2 activates PIK3CA, MFN1 and OPA1 transcription. PIK3CA or downstream AKT pharmacological inactivation impairs SOX2 nuclear localization and aggravates SOX2 turnover. This indicates a positive regulation loop where AKT signaling activates SOX2 function, which in turn activates PIK3CA transcription and also MFN1 and OPA1. 3q26 copy number variations in 100 glioma biopsies show frequent SOX2 gain (29%) and OPA1 loss (32%). SOX2 amplification is consistent with the transcriptional activation of known oncogenic targets, including PIK3CA. OPA1 loss is consistent with increased invasion relevant to mitochondria fragmentation. Thus, SOX2 activates oncogenic and tumor suppressor target genes. While the oncogenic ones (PIK3CA) are kept 'on', OPA1 needs to be turned 'off'. Copy number variations of 3q26 genes are currently being tested for impact on patient survival and tumor invasion status.

Conclusion

We provide evidence that a regional interplay between 3q26 genes promotes glioma invasion. Copy number variations of individual genes suggest optimization of oncogenic activities.

009

ACE-Inhibitors - a preventive measure for bone flap resorption after autologous cranioplasty in hypertensive patients?

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Object

Bone flap resorption (BFR) is a long term complication after autologous cranioplasty (AC). This study investigates risk factors for BFR after AC including medical conditions and antihypertensive drug therapies, which have been associated with bone metabolism in orthopedic and osteoporosis research. Angiotensin-converting enzyme inhibitors (ACEI) are known to be associated with a beneficial effect on bone healing and bone preservation.

Methods

In this retrospective exploratory study, clinical and radiographic data of 158 patients who received AC after decompressive craniectomy (DC) between June 2003 and August 2015 at the Department of Neurosurgery at the University Hospital in Bern, Switzerland, were evaluated. Information on bone flap, patient demographics, dates of surgeries, medical conditions and antihypertensive therapy was collected. BFR was defined by a clinical or radiographic diagnosis with indication for a revision surgery established by a neurosurgeon. A Kaplan-Meier analysis of time from surgery to diagnosis of BFR was performed and factors associated with BFR were investigated using the log-rank test and Cox regression.

Results

Overall median follow-up time was 1.36 years (interquartile range, IQR 0.40-2.52) and BFR occurred in 47 patients (29.7%) after a median time of 0.98 years (IQR 0.53-2.27). Kaplan-Meier method and log-rank test revealed an association between lower BFR rates and intracerebral bleeding (ICB, HR 0.200, 95%CI 0.048-0.828, $p=0.014$), ventriculo-peritoneal shunt (VP-Shunt, HR 0.379, 95%CI 0.158-0.907, $p=0.024$) and ACEI therapy (HR 0.395, 95%CI 0.175-0.891, $p=0.020$). Cox regression confirmed antihypertensive therapy with ACEI (HR 0.175, 95%CI 0.049-0.627, $p=0.007$), VP-shunt (HR 0.264, 95%CI 0.096-0.727, $p=0.010$) and ICB (HR 0.195, 95%CI 0.044-0.863, $p=0.031$) to have a significantly lower risk for BFR as well as male gender (HR 0.488, 95% CI 0.250-0.953, $p=0.036$).

Conclusion

This is the first study that demonstrates a lower rate of BFR in patients receiving ACEI, which is in line with previous reports on the positive influence of ACEI on bone healing and preservation. ACEI, given as hypertensive medication, is to our knowledge the only modifiable factor to lower the rate of BFR after AC. Further investigations may consider the bone flap preserving effects of ACEI when treating DC patients who require hypertensive medication.

010

Use of Subperiosteal Drain versus Subdural Drain in Chronic Subdural Hematomas treated with Burr-Hole Trepanation: a randomized controlled trial

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Background

Chronic subdural hematoma (cSDH) is one of the most frequent neurosurgical entities. The use of a subdural drain after burr-hole trepanation for cSDH was proven to reduce recurrence and mortality at 6 months. To date in neurosurgery practice evidence based guidelines on what kind of drain should be used, namely a subdural or subperiosteal drain, do not exist. Currently both methods are being practiced depending on the institute and/or the practicing neurosurgeon. The aim of this study is to compare the reoperation rates after burr-hole trepanation and insertion of a subperiosteal or subdural drain in patients with cSDH.

Methods

We conducted a prospective, non-inferiority, multi-center, randomized controlled study designed to include patients above the age of 18 years, presenting with a symptomatic cSDH verified on cranial CT or MRI, who are to undergo surgical evacuation with burr-hole drainage. After obtaining informed consent patients were randomly allocated to a subperiosteal drain (SPD) group or a subdural drain (SDD) group. The primary endpoint was recurrence indicating a reoperation within 12 months. Sample size was set at 220 patients to ensure with 80 % power the estimation of a 95% confidence interval which is entirely below the predefined non inferiority margin of Δ 3.5%.

Results

220 patients were recruited and randomized to the SPD and SDD group. So far the 6 weeks follow up has been completed, (first follow up period), while the 12 months follow up is expected to be completed in January 2017. We will present our preliminary results of the primary and secondary outcome measurements for the first follow up period (6 weeks).

Conclusions

To date evidence based recommendations concerning the operative treatment of cSDH are sparse. Results of this study will provide us with class I evidence for one of the most frequent treatment modalities of cSDH.

Trial Registration: ClinicalTrials.gov: NCT01869855

O11

Aneurysm surgery after 3D planning in a Virtual Reality environment: Technique and outcome analysis in 115 cases

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Objective

Aneurysm surgery demands precise spatial understanding of the vascular anatomy and its surroundings. We report on a decade of experience planning clipping procedures pre-operatively in a virtual reality (VR) workstation and present outcomes with respect to mortality, morbidity and aneurysm occlusion rate.

Methods

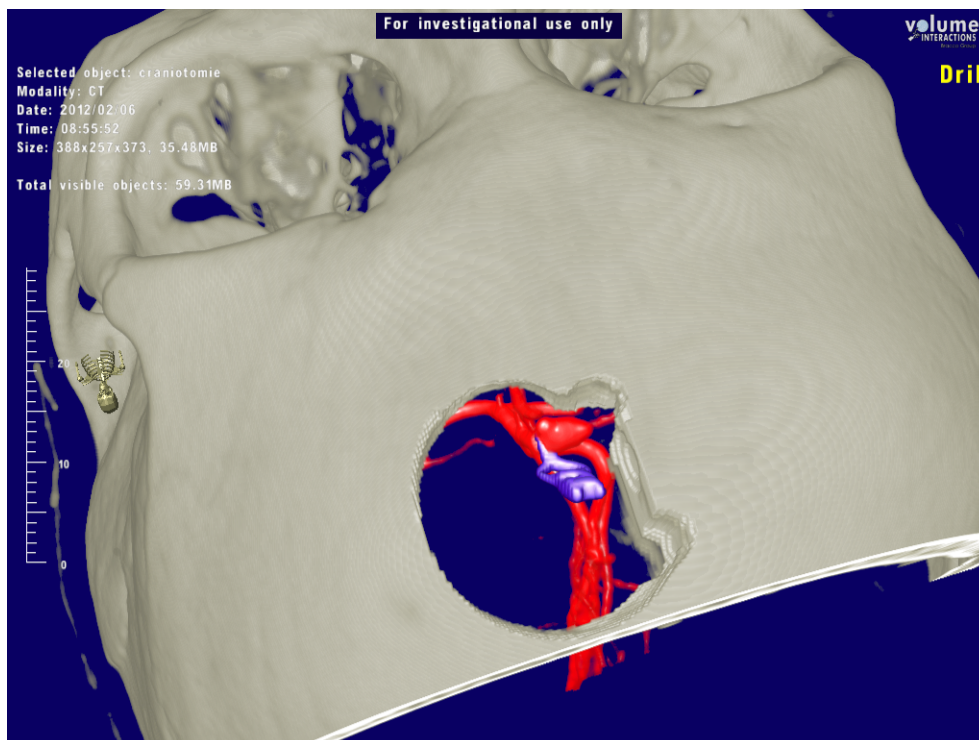
The clipping of 115 intracranial aneurysms in 105 patients was pre-operatively planned with the Dextroscope, a stereoscopic, patient-specific VR environment. Outcome data for all cases, planned and performed in three institutions by surgeons at various stages of their neurovascular learning curve, was analyzed based on clinical charts and radiological reports.

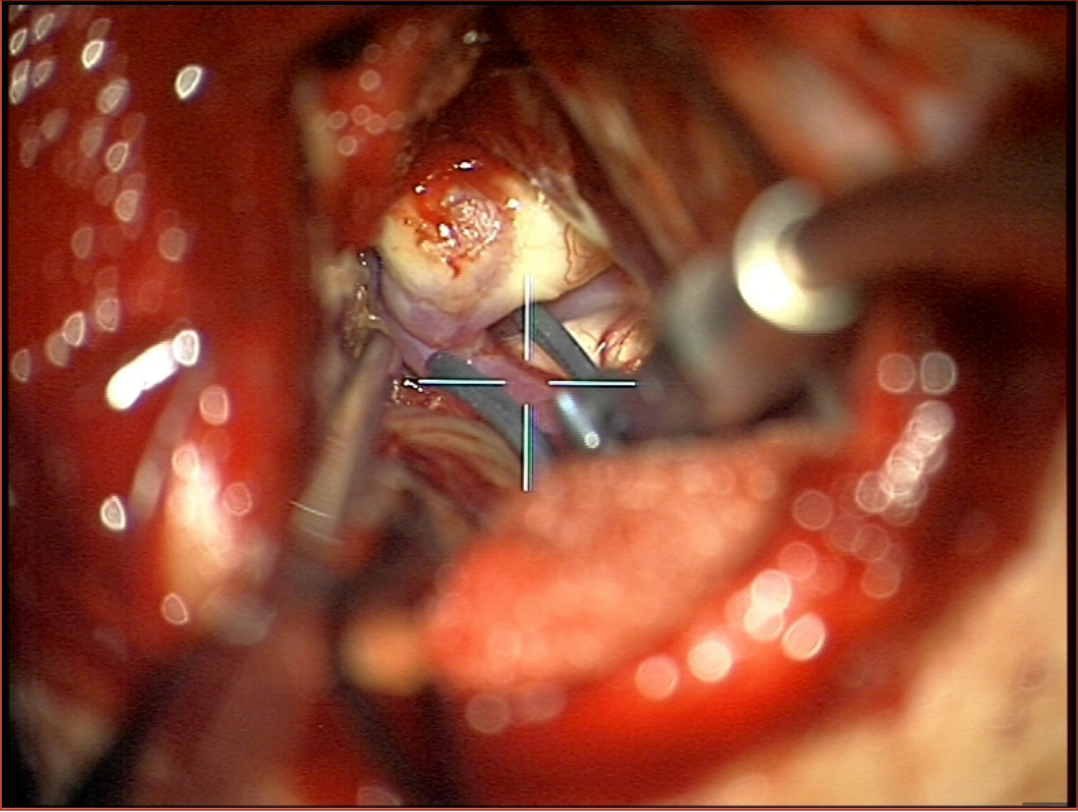
Results

85 incidental, unruptured aneurysms in 77 patients were electively planned and treated surgically. Mortality was 0% and morbidity (mRS>2) was 2.6%. The rate of complete aneurysm obliteration on post-operative imaging was 91.8%. In addition, 30 aneurysms were treated in 28 patients with prior subarachnoid hemorrhage. Mortality in these cases was 3.6%, morbidity (mRS>2) 7.1% and the rate of complete aneurysm clipping was 90%. In the consecutive sub-cohort of patients operated on by neurosurgeons in early neurovascular training, occlusion rates of 93.7% and 92.6% were achieved in the unruptured and ruptured cases respectively, with morbidity of 0% and 8%.

Conclusion

Meticulous 3D surgical planning in a VR environment enhances the surgeon's spatial understanding of the individual vascular anatomy and allows clip preselection and positioning as well as anticipation of potential difficulties and complications. In comparison to other aneurysm cohorts, including ISAT, BRAT and ISUIA, VR planning was associated with better clinical outcomes while maintaining equivalent closure rates.





012**Intraoperative monitoring of visual evoked potentials**

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Objective

To determine the predictive values of intraoperative visual evoked potentials (VEP) change that best predict postoperative visual field defects and to evaluate the usefulness of VEP to prevent these defects.

Methods

VEP were elicited with the NimEclipse system using white led (Medtronic, Minneapolis, MN, USA) and were protected from scialytic light. VEP were monitored for 32 patients undergoing resection of brain lesions. Localization of these lesions was divided into three groups: fronto-temporo or parietal, occipital and fronto-basal (N=14 patients, N=2, N=9 respectively). Postoperative cerebral hemorrhage, ischemia or cytotoxic edemas (N=5) were excluded. VEP of n=40 eyes in N=25 patients were reliably recorded and analysed. Electroretinography (ERG) was performed to confirm retinal light stimulation for all patients. The neurosurgeon was warned with an alarm when the amplitude of the VEP decreased below 20%. Visual fields were assessed preoperatively and at one month after surgery by clinical appointments and Goldmann perimetry.

Results

In 93% of patients (25/27) and in 74% of eyes (40/54), reliable VEP and ERG were recorded. In 63% of eyes (25/40) no postoperative visual changes were observed and no alarm was given (true negative). In 30% of eyes (12/40) new visual field defects were observed postoperatively when this alarm was given (true positive). The threshold of 15% to give an alarm correctly identified 100% of all eyes with postoperative visual changes (sensitivity). Unchanged VEP amplitude correctly identified 89.3% of all eyes that do not have visual changes (specificity). Positive alarm predicted a postoperative visual impairment in 80% of cases (positive predictive value). The absence of alarm predicted an absence of postoperative visual impairment in 100% of cases (negative predictive value). In 23% of eyes (9/40) and in 28% of patients (7/25) transitory loss of VEP were observed with a total recovery at the end of the surgery without postoperative visual defects.

Conclusion

Reliable intraoperative VEP can only be monitored when electroretinography is added in neuromonitoring protocol. This gave alarm criteria of 20% of decrease of VEP and predicts visual change after brain lesions resection. Moreover, stable VEP were obtained by carefully protecting the light stimulation of the patient eyes by the light of the scialytic and microscope.

013

Intended Near-Total Removal of Koos Grade IV Vestibular Schwannomas: A Need to Revisit Treatment Paradigms?

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Background

Koos IV vestibular schwannomas are typically managed by surgical resection with completeness of resection being the goal. To maximize good functional outcome we propose a paradigm shift towards intended subtotal removal where a small amount of mainly tumor capsule is intentionally not dissected of the particularly fragile cisternal portion of the facial nerve. Patients are then followed by a wait-and-scan approach with repeat debulking or stereotactic radiosurgery in case of clinical or volumetric progress.

Material and methods

Forty-four consecutive patients underwent intended subtotal resection of a newly diagnosed Koos IV vestibular schwannoma between January 2009 and December 2015. Mean patient age was 58years (range 22.6–84.3years). Mean pre-operative tumor volume was 12.3cm³ (range 2.2–65.8cm³). Pre-operative facial-nerve-function was good (HB I-II) in 43 cases (97%), or fair (HB III) in the remaining case (2%). All patients underwent routine neurological testing and MRI imaging at three months, one year, and annually thereafter. Volumetric analysis was performed using routine MRI sequences (CISS and T1-Gd) and the Brainlab®Cranial 3.0 software.

Results

At mean 36.2months follow-up, facial function was good (HB I-II) in 88.6%, fair (HB III) in 6.8%, or poor (HB IV-VI) in 4.5% of patients. The volumetric extent of resection at first follow-up (mean 0.7month) was 75.7% with a residual of mean 3.0cm³ (range 0–6.3cm³), and increased to 88.0% at last follow-up with a remnant of mean 1.48cm³. Over the entire follow-up period, tumor remnants regressed in 68%, remained stable in 7%, and progressed in 25% of cases. Of the 7 remnants that showed clinical or radiological progression, 5 were referred to stereotactic radiotherapy and 2 underwent repeat surgical resection.

Conclusion

Intended total removal of large or very large vestibular schwannoma offers prime facial nerve function outcome. The few tumor remnants that show clinical or volumetric progression over time can be addressed by repeat surgical debulking or stereotactic radiosurgery.

014**Low frequency microstimulation in patients with epilepsy does not produce inhibition but stimulator can**

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Deep brain stimulation (DBS) is applied to control symptoms of neurological diseases such as movement disorders or refractory epilepsy. DBS is applied in many different cerebral targets and its mechanisms of actions remain debated. The goal of the present study is to study these mechanisms by analyzing the effects of microstimulation on the activity of neurons at the site of stimulation, in patients with refractory epilepsy. Microelectrode recordings were performed before, during and after microstimulation in seven patients with refractory epilepsy (five patients with hippocampal abnormality; two patients with cortical dysplasia). Neuronal spikes could be extracted from multi-unit recordings successfully with clustering in four patients with hippocampal and in one patient with cortical microstimulation (1Hz, charge-balanced biphasic waveform, 60 ms/ph, 25 mA). The firing rate increased significantly during microstimulation in five out of seven available periods of microstimulations ($p < 0.001$). The firing rate remained higher than before stimulation after all sets of microstimulation ($p < 0.001$). In vivo human microstimulation was hence sufficient to induce neuronal excitation with significant increases in firing rate, lasting beyond the stimulation. Hippocampal excitation of microstimulation is in agreement with epileptogenic effects of low frequency macrostimulation. This is usually not reported in animal-model studies. Indeed many of them, as others in the domain of movement disorders, suggest inhibition as a mechanism of action of DBS. Nevertheless these studies were conducted applying non-charge balanced stimuli which can produce inhibition of neurons consequently to electrochemical reactions at the interface of the electrode. On the contrary charge balanced stimuli are mandatory for chronic DBS to avoid local brain lesions. Therefore inhibition reported as a mechanism of action of DBS is overestimated in the literature and excitation may still be underestimated as a mechanism of action of safe DBS.

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015

Prevalence of complications in intraoperative MRI combined with neurophysiological monitoring.

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Background

High field intraoperative MRI (ioMRI) is becoming increasingly available in neurosurgery centers, where it has to be combined with intraoperative neurophysiological monitoring (IONM). IONM needle electrodes remain on the patient during ioMRI and may cause image distortions and burns.

Objective

We tested MR-heating experimentally and investigated the prevalence of complications.

Methods

We studied electrodes that are certified for IONM, but not “MR conditional”. They consist of copper cables (length 1.5 m) and needles made of either stainless steel (ferromagnetic) or Pt/Ir (paramagnetic). We simulated an ioMRI session with gel and measured the temperature increase with optical fibers. We measured the force an electrode experiences in the magnetic field. We prospectively documented subcutaneous needle electrodes between 2013-2016 that remained on the patient during intraoperative 3 Tesla ioMRI scans.

Results

The in-vitro testing of the electrodes produced a maximum heating $\Delta T = 3.9^{\circ}\text{C}$ and force of 0.026 N. We placed 1237 subcutaneous needles in 57 surgical procedures with combined IONM and ioMRI, where needles remained placed during ioMRI. One patient suffered from a skin irritation at the shoulder. All other electrodes placed had no side effects.

Conclusions

We have corroborated the history of safe use for electrodes with 1.5 m cable and demonstrate their use. Nevertheless, heating cannot be excluded, as it depends on location and cable placement. When leaving electrodes in place during ioMRI, risks and benefits have to be carefully evaluated for each patient.

O16**The validity of the timed-up-and-go (TUG) test as an outcome measure in degenerative disc disease**

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Background

As previously reported, the timed-up-and-go (TUG) test is a reliable tool to evaluate objective functional impairment (OFI) in patients with degenerative disc disease. The aim of this study is to assess the validity of the TUG test to measure change in function postoperatively.

Methods

In a prospective two-centre study, OFI was assessed by the TUG test in patients scheduled for lumbar spine surgery, on postoperative day 3 (D3) and 6 weeks (W6). The TUG tests were correlated with established subjective measures of pain intensity (Visual Analogue Scale (VAS) for back and leg pain), functional impairment (Oswestry Disability Index (ODI)) and health-related quality of life (HRQoL) (Short Form-12 (SF12)).

Results

The patient cohort comprised n=100 patients with a mean age of 56.2 years. N=57 were males; n=45 had a microdiscectomy for lumbar disc herniation, n=35 a decompression for a lumbar spinal stenosis and n=20 a fusion procedure. The OFI t-score was 122.1 before surgery. Postoperatively, it fell to 117.9 and 102.9 at D3 and W6, respectively. The Spearman Correlation Coefficient (SCC) for the TUG test and VAS back pain was 0.18 preoperatively and 0.31 at W6. The SCC for the TUG test and the ODI was 0.45 preoperatively and 0.43 at W6. The SCC for physical HRQoL (SF12) was -0.16 preoperatively and -0.28 at W6.

Conclusions

The TUG test is sensitive to change, reliably reflects the postoperative functional outcome and correlates with subjective measures of pain, functional impairment and HRQoL. It may thereby complement a comprehensive pre- and postoperative assessment.

017

Low-Dose Acetylsalicylic Acid and Bleeding Risks with Ventriculoperitoneal (VP) Shunt Placement

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Object

Ventriculoperitoneal (VP) shunt is a common procedure for the treatment of hydrocephalus following diverse neurosurgical conditions. Many of the patients present with other comorbidities and receive antiplatelet therapy, usually Acetylsalicylic acid (ASA). Despite its clinical relevance, the perioperative management of these patients has not been sufficiently investigated. The aim of this study is to compare the peri- and postoperative bleeding complication rates in patients undergoing VP-shunt placement associated with ASA intake.

Methods

Out of 172 consecutive patients undergoing VP-shunt placement from June 2009 to December 2015, 40 (23.3%) patients were under low-dose ASA treatment. The primary outcome measure was bleeding events in ASA users vs. nonusers, while secondary outcome measures were postoperative cardiovascular events, hematologic findings, morbidity and mortality. A sub-analysis was conducted in patients discontinuing ASA treatment for <7 days (4 cases (10%, 3 females, 75 %)) (ASA group 1) and for ≥7 days (n=36, 90%; 9 females, 25%) (ASA group 2) postoperatively comparing bleeding complication rates.

Results

No statistically significant difference for bleeding events was observed between ASA users and nonusers ($p=1$). Cardiovascular complications, surgical morbidity, and mortality did not significantly differ between the groups, either. Moreover, there was no association between ASA discontinuation regimen (<7 days and ≥7 days postoperatively) and hemorrhagic events.

Conclusion

Given the lack of guidelines regarding perioperative management of neurosurgical patients with antiplatelet therapy, our findings elucidate one issue, showing comparable bleeding rates in ASA users and nonusers undergoing VP-shunt placement.

O18**Personality traits in neurologists, neurosurgeons and psychiatrists**

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Background

Since the beginning of clinical neuroscience, three major specializations coexist and collaborate in daily patient care: neurology, neurosurgery and psychiatry. Different personality traits have traditionally been attributed to each of these three. But is this a reality? And if yes, do these personality traits influence our career choice, or do they appear during and as a result of our specialization?

Methods

An online survey was sent out to board-certified specialists, residents and medical students in several European and Northamerican countries between 02/2016 and 05/2016. It addressed age, sex, primary language, educational level and speciality. Participants filled out the ten-item personality inventory (TIPI), a validated measure of the Big Five personality dimensions, the best accepted and most commonly used model of personality in academic psychology.

Results

A total of n=5148 complete datasets were received, of which only data of responders indicating the specialties neurology (n=283), neurosurgery (n=205) and psychiatry (n=287) were included. A total of n=315 responses (40.7%) were from board-certified specialists. With regard to them, the n=84 neurosurgeons scored higher on the item emotional stability than both the n=109 neurologists ($p=0.009$) and the n=122 psychiatrists ($p=0.080$), while there was no difference between neurologists and psychiatrists. Conscientiousness was highest in neurosurgeons, followed by neurologists and psychiatrists with neurosurgeons and psychiatrist differing significantly ($p=0.064$). There were no significant group differences in the degree of agreeableness, extraversion and openness to experience. Broadly overlapping 95% CIs of the difference of z-scores for any of the Big Five between specialists, residents and medical students choosing a sub-specialty indicate that the relationships are stable over all three educational levels.

Conclusion

There are small but significant differences in personality traits between neurosurgeons and both neurologists and psychiatrists, respectively. No differences were found between neurologists and psychiatrists. In general, all three sub-specialties diverged in a similar manner from the normal population benchmark, indicating that all three medical sub-specialties share common characteristics that make them distinct from the general population. Personality traits might influence the choice of medical specialty.

019

Antithrombotic medication and bleeding risk in patients with cerebral cavernous malformations: a cohort study.

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Introduction

Data about the risk of long-term antithrombotic medication (ATM) in patients with cerebral cavernous malformations (CCMs) are scanty. The aim of this study was to determine the hemorrhagic risk associated with ATM in patients diagnosed with CCMs.

Methods

Demographic (age, gender), clinical (presentation with hemorrhage, infratentorial location, brainstem location, history of high blood pressure), treatment and ATM informations of patients diagnosed with CCMs in a single institution between 1980 and 2015 were retrospectively collected. Multivariate descriptive and survival analysis were performed, looking at potential risk factors associated with CCMs related hemorrhage. Variables that may influence the risk of de novo hemorrhage were assessed using Cox proportional hazard regression analysis from referral until the first occurrence of the following: de novo hemorrhage, treatment or last review.

Results

A total of 408 patients harboring 542 CCMs were included in the analysis of the risk of hemorrhage. Of those, 51 CCMs were seen on only one occasion, leading to a total of follow-up of 1625 lesion-years. 82 patients harboring 90 CCMs (17%) were on ATM, with a total follow-up of 138 lesion-years. Hemorrhage at the time of diagnosis was found in 136 (25%) CCMs, while 37 (7.5%) CCMs bled during follow-up, leading to a 2.3% annual risk of CCMs de novo hemorrhage. In multivariate logistic regression, younger age and brainstem location were the only factors associated with both CCMs hemorrhage at presentation [(OR 0.99; 95%CI 0.98-0.99) and (OR 1.97; 95% 1.14-3.42)] and de novo CCMs hemorrhage during follow-up [(OR 0.97; 95%CI 0.95-0.99) and (OR 2.86; 95%CI 1.24-6.59)]. This was confirmed by multivariate Cox regression survival analysis, where age (HR 0.977; 95%CI 0.958-0.996) and brainstem location (HR 2.51; 95%CI 1.13-5.57) were the only variables associated with a shorter time to de novo CCMs hemorrhage during follow-up. ATM was found not to be associated with an increased risk of CCMs hemorrhage at presentation, nor with an increased risk of de novo CCMs hemorrhage during follow-up in both descriptive and survival analysis.

Conclusions

Antithrombotic medication does not seem to be associated with an increased risk of hemorrhage in patient diagnosed with cerebral cavernous malformations. However, the use of antithrombotic medication in younger patients and/or in those with brainstem-located cavernous malformations should be evaluated with caution.

O20**Influence of Postoperative Thrombosis Prophylaxis on the Recurrence of Chronic Subdural Hematoma after Burr-hole Drainage**

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Objective

Chronic subdural hematoma (cSDH) is a commonly encountered disease in neurosurgical practice while its increasing prevalence is compatible with the ageing population. Recommendations concerning postoperative thrombosis prophylaxis (TP) after burr-hole drainage of cSDH are lacking. The aim of this study was to analyze the correlation between recurrence of cSDH and postoperative application of TP.

Methods

We retrospectively analyzed data from 234 consecutive patients undergoing surgical evacuation of cSDH via burr hole craniostomy followed by drain insertion at our institution between January 2013 and March 2016. Following variables were collected and recorded: postoperative TP, time (< 48h vs. > 48h) and dosage of application, postoperative thromboembolic and cardiovascular events, as well as demographic parameters, comorbidities, preoperative treatment with anticoagulants and antiplatelets, and laboratory parameters. The primary endpoint was re-operation of cSDH due to recurrence..

Results

Overall cSDH recurrence rate was 12.7%. Out of the 234 analyzed patients, 135 (57.3%) received postoperative TP. Recurrence rate did not differ between both groups ($p=0.077$). A sub-analysis comparing recurrence rate dependent on the application time of TP (< 48h vs. > 48h) showed no significant difference either ($p=0.098$).

Conclusions

Our data suggest that the application of postoperative TP after burr-hole drainage for cSDH does not result in higher recurrence rates. In addition, it seems that early administration of TP (<48h) has no effect on recurrence rates.

021

Perioperative Management of Anticoagulant - and Platelet - Inhibiting Medications in Patients Undergoing Elective Spine Surgery – Results From a Nationwide Survey

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Background

Perioperative use of anticoagulant and platelet inhibiting agents in patients undergoing spine surgery poses the dilemma of increased risk of hemorrhage as opposed to an increased risk of thrombosis or complications by discontinuing the patients anticoagulant or platelet inhibiting medications. The aim of this study was to examine the standards, expert opinions through a nationwide survey.

Method

Web based survey by invitation. Invitations with a personal token to access the survey were sent to one representative of each neurosurgical - and orthopaedic unit performing spine surgery and to all other active surgeon members of the Swiss society of neurosurgery or Swiss society of spinal surgery. 97 e-mail invitations were sent to 19 representatives of neurosurgery or orthopaedic units and 78 registered neuro- and orthopaedic surgeons potentially performing spine surgery.

Results

From February to April 2016 42 surgeons (26 Neurosurgeons, 16 Orthopaedic Surgeons) completed the survey (43%). 14 (74%) of the invited 19 unit representatives and 26 (33%) of the 78 attending surgeons completed the survey. 61% prescribe prophylactic heparin preoperatively and depending on the procedure 83-90% postoperatively. 38% restart/commence it 6 hours postoperatively, 35% on the day of surgery and 25% on the 1st postoperative day. Depending on the type of surgery 23-48% discontinue acetylic acid preoperatively, while 80-88% always discontinue clopidogrel preoperatively. An additional 7-15% discontinued clopidogrel only if in addition to acetylic acid. Resumption of platelet inhibition on average is 4.1 ± 2.6 days postoperatively. Orthopaedic surgeons recommence platelet inhibition earlier than neurosurgeons ($p=0.013^*$). Anticoagulation with Rivaroxaban was discontinued 3 ± 2 days before surgery. Only 41% of respondents routinely replace it with heparin when ceased, while 36% always consult an internist to make a decision. 25% measure preoperative anti-Xa-activity routinely and 19% depending on other factors. Discontinued traditional anticoagulation (Vitamin K antagonists) is, depending on the indication, temporarily replaced in the perioperatively with heparin by 71.8-97.5% of respondents.

Conclusion

Administration and discontinuation of anticoagulant and platelet inhibiting medications in the perioperative setting of spinal surgery vastly differs between different centres and surgeons. No clear reasons for these differences could be determined.

022

Vulnerable plaques in mild carotid stenosis: the risk of stroke

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Purpose

First evaluation of a 3D black blood fat-saturated FSE T1-weighted sequence for the detection of intra-plaque hemorrhage (IPH) in symptomatic individuals, with investigation of the relation between severity of stenosis and diffusion weighted imaging (DWI) positive ischemic lesions.

Methods

62 patients (37-89 years; average, 74 years) were studied on a 3T PET/MR unit. The acquisition protocol comprised axial DWI, echo-gradient T2, and coronal FLAIR sequences of the brain, as well as 3D TOF and 3D FSE T1 black blood sequences at the level of the carotid bifurcations, the latter to detect IPH, presenting as a focal hyperintensity. Both common and internal carotid arteries (ICA) were analyzed in each patient, and the NASCET scale was used for quantification of the degree of carotid stenosis.

Results

36 out of the 62 patients showed areas of ischemia on DWI. 15 of these 36 patients (42%) had associated ipsilateral IPH either at the carotid bifurcation, or the proximal ICA. The mean degree of stenosis in this group was 49%. In 21 patients with ischemia without intra-plaque hemorrhage, the mean degree of stenosis was almost identical at 48%.

Conclusion

MR with black blood fat-saturated FSE T1 technique is a safe, reliable, and non-invasive tool for the detection of IPH. Our study demonstrates that a high percentage (42%) of ischemic events in patients with mean low-degree stenosis (<50%) are associated with IPH, an easily detectable imaging marker of vulnerability. The capacity to detect intra-plaque hemorrhage will help in stratifying patients into different risk groups.

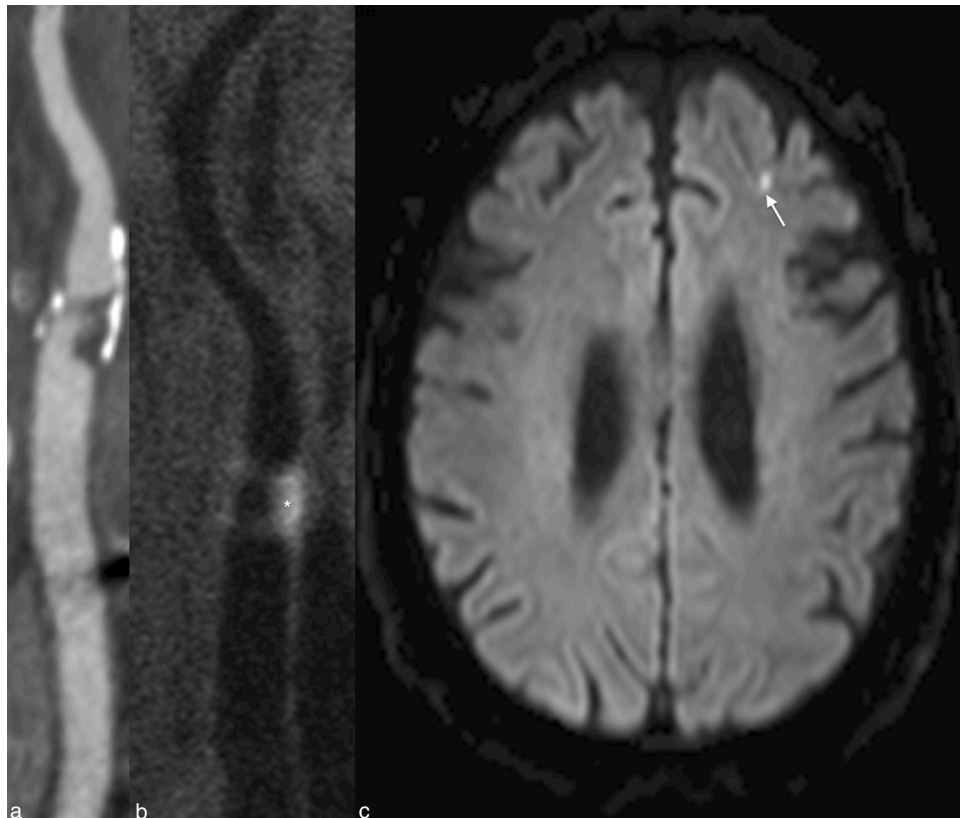


Fig 1

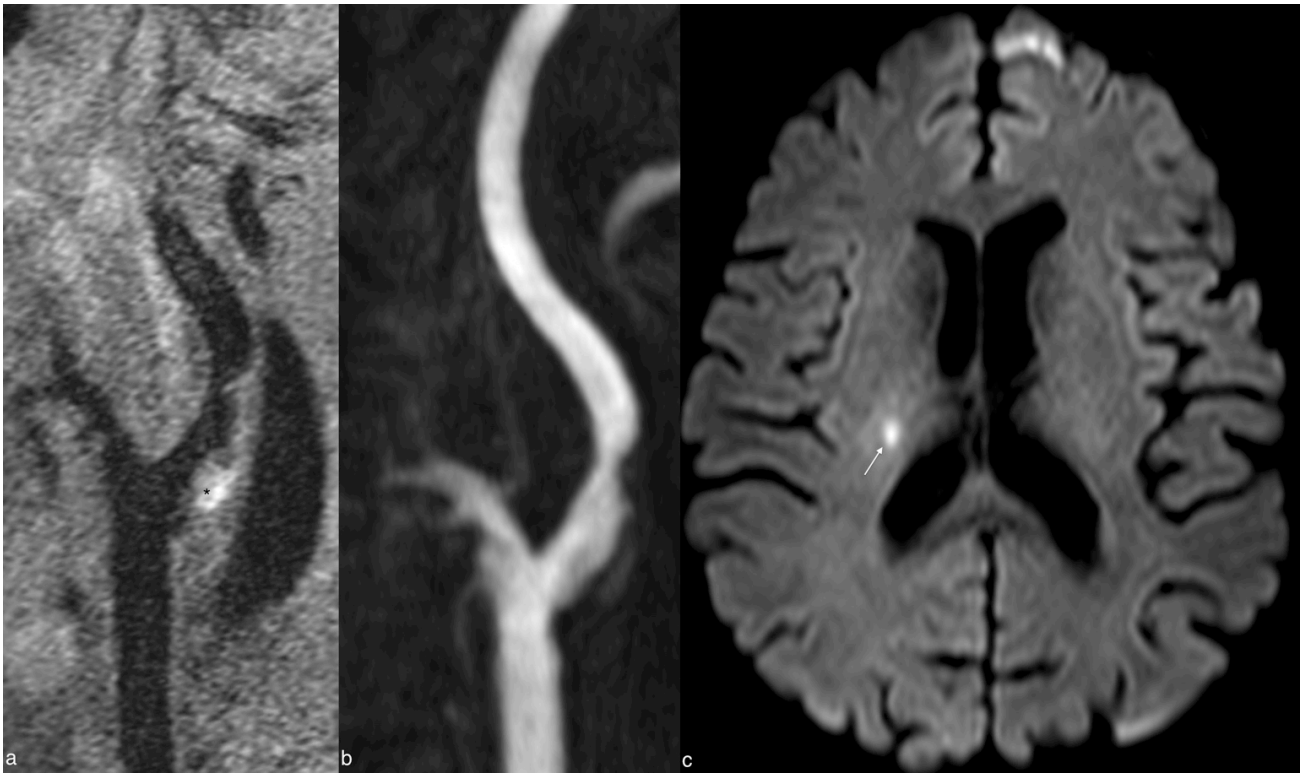


Fig 2

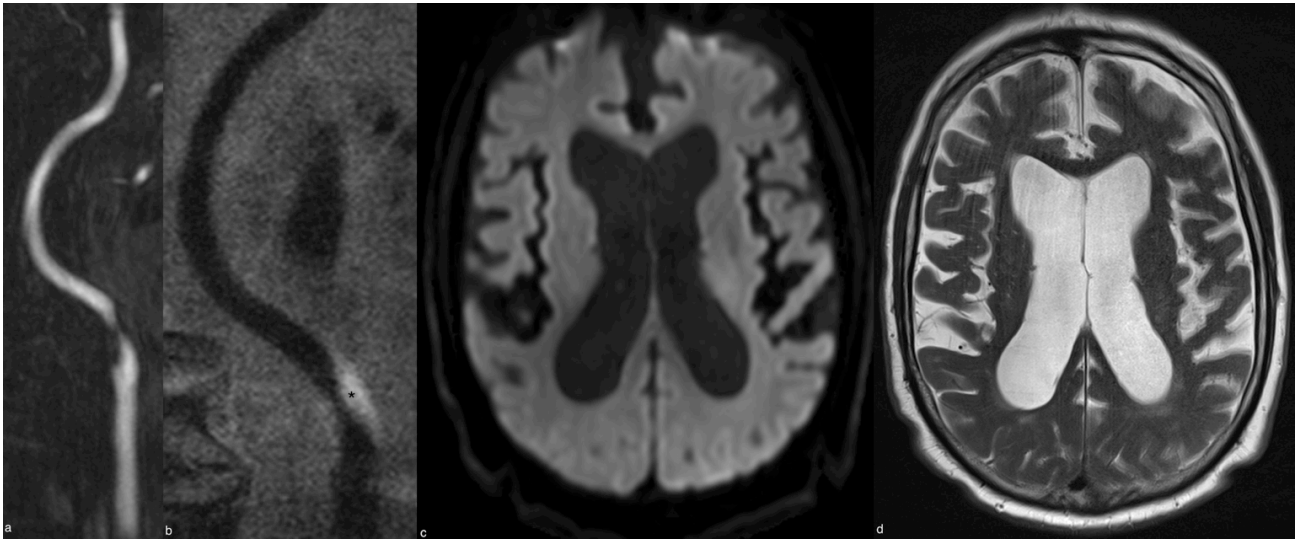


Fig 3

O23**Dynamic Flexion-Extension Diffusion-Tensor Weighted Imaging of the Cervical Spine: A feasibility study.**

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Background and purposes

In compressive cervical myelopathy MRI in neck flexion or extension reveals T2-weighted signal changes which are not apparent in the neutral position. Furthermore, diffusion tensor imaging (DTI) has been reported to show a higher sensitivity than conventional T2-weighted imaging for the detection of myelopathy. In this study, the feasibility and reproducibility of dynamic flexion-extension DTI in the cervical spinal cord was assessed in healthy volunteers.

Materials and Methods

Eleven healthy volunteers were enrolled in the study. A cervical spine examination with T2 and DTI sequences was performed using a 3T MRI-scanner. The examination was then repeated in maximum neck flexion-extension. Fractional anisotropy (FA) and apparent diffusion coefficients (ADC) were calculated and compared between the extended, neutral and flexed neck positions. Measurements are provided as mean $\pm$ SD.

Results

The average range of motion within extension-flexion was $54.7\pm 11.3^\circ$. Spinal canal diameters were smaller in extension (11 ± 2 mm) compared to neutral position (12 ± 2 mm) and flexion (12 ± 2 mm; $p<0.01$) especially in segments C4/5 and C5/6. Respective FA and ADC values at C4/5 in flexion (649 ± 77 ; 1256 ± 116), neutral position (651 ± 55 ; 1242 ± 111) and extension (653 ± 65 ; 1208 ± 148) did not differ significantly.

Conclusion

Flexion-extension DTI of the cervical spine was well tolerated in healthy volunteers. Moreover, FA and ADC values were reproducible and correlated well when compared between flexion, neutral position and extension. The present findings encourage a trial of dynamic DTI in patients with cervical spondylotic myelopathy.

024

Comparison between Indocyanine Green Videoangiography and intraoperative Digital Subtraction Angiography

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Aims

Intracranial aneurysm (IA) surgery aims at complete aneurysm obliteration yet preserve the parent arteries. Intraoperative indocyanine green videoangiography (ICGA) has been successfully introduced during the last decade to obtain real-time high-resolution images of surgically exposed cerebral vasculature. The aim of the study is to assess the practical application of ICGA during IA surgery in comparison with 3D intraoperative digital subtraction angiography (iDSA).

Methods

We retrospectively reviewed 140 patients that underwent IA surgery in a hybrid operating room between November 2011 and February 2015. Number, size, and location of IA, ICGA and iDSA findings, and the need for intraoperative clip adjustment after ICGA and iDSA were recorded. Discordance between ICGA and iDSA was defined as ICGA demonstrating aneurysm obliteration and normal vessel flow, but subsequent iDSA showing either an aneurysmal remnant and/or parent artery occlusion requiring clip adjustment.

Results

ICGA and iDSA was applied in 120 patients with maximal IA size of 23mm. Out of these 27 had intraoperative clip repositioning. The clip adjustment after visual inspection alone was 30% (8 out of 27), adjustment after ICGA was 52% (14 out of 27) and after iDSA 18% (5 out of 27). Reasons of clip adjustments were aneurysm remnants, parent artery occlusion, atheromatose plaques, vessel rupture, or residual perfusion in either ICGA or iDSA. A non-correspondence between ICGA and iDSA was described in 5,8% (7 out of 120). Five out of seven aneurysms were located at the arteria communicans complex.

Conclusion

Although overall non-correspondence between ICGA and iDSA was relatively low (5.8%) 3D-iDSA seems to improve diagnostic yield for the intraoperative detection of parent artery compromise and/or persistent residual IA.

025

Low-noise amplifier improves fast ripple detection in ECoG during epilepsy surgery

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Rationale

Fast ripples (FR) in the intraoperative electrocorticogram (ECoG) have recently been shown to be specific predictors of outcome of epilepsy surgery. FR detection is restricted by their low signal-to-noise ratio (SNR) and time consuming visual marking. We present here the combination of a low-noise recording system with a semi-automatic detection of high-frequency oscillations (HFO).

Methods

We recorded intraoperative ECoG (9 patients, 5722 minute recordings total, 135 channels) simultaneously by a commercial device (CD, input noise level 21 nV/ $\sqrt{\text{Hz}}$) and by a custom-made low-noise amplifier (LNA, input noise level 2.3 nV/ $\sqrt{\text{Hz}}$). The HFO analysis was conducted separately for ripples (80-250 Hz) and FR (250-500 Hz). The automatic detector performed first an entropy-based computation of baseline amplitude and then a detection of HFO events in the time-frequency domain. All events were visually validated by three independent reviewers. Channels with >1 event/min were counted as indicative of poor outcome.

Results

Over all channels, the baseline amplitude was 4.6 ± 3.0 μV for ripples and 2.0 ± 1.4 μV for FR in CD and 4.8 ± 7.1 μV for ripples and 1.3 ± 0.8 μV for FR in LNA. Ripple rates were 4.4 ± 6.8 events/min in CD and 7.9 ± 15.9 in LNA ($p < 0.001$). FR rates were 0.2 ± 0.5 events/min in CD and 0.9 ± 1.5 in LNA ($p < 0.001$). Across patients, the similarity of spatial patterns between CD and LNA was 0.76 ± 0.3 for ripples and 0.2 ± 0.4 for FR. In post-resection ECoG of the 7 patients with available outcome, FR were found in 2/7 patients in LNA recordings, while no FR were found in CD. This resulted in PPV = 0% and NPV = 57%, CI [18-90] in CD; and PPV = 100%, CI [15-100] and NPV = 80%, CI [28-99] in LNA.

Conclusions

Low-noise recordings enhance the SNR in the FR range. The combination of optimized acquisition system and semi-automatic HFO analysis improved FR detection. The opportunity to detect a higher amount of FR represents a critical advance in evaluating the benefit of FR in clinical application.

027

The value of short-term pain relief in predicting the 1-month outcome of lumbar transforaminal epidural steroid injections

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Objective

To determine whether short-term leg pain alleviation following computed tomography-guided transforaminal epidural steroid injections can predict the 1-month outcome.

Design

Prospective observational. Setting: Tertiary radiology department. Subjects: n=57 consecutive patients with radiculopathy secondary to a lumbar disc herniation.

Methods

Study components were visual analog scale leg and back pain at baseline, 15, 30, 45 minutes, 1, 2, and 4 hours, on days 1-14, as well as at 1 month. Health-related quality of life and functional impairment were assessed using the short form-12 and Oswestry disability index. Patients who reported >80% persisting leg pain, as well as patients who underwent a second injection or an operation within 1 month were defined as 'non-responders'. Logistic regression was used to analyze the effect size of the relationship between >50% pain relief at any given study visit and responder status.

Results

Patients experiencing a >50% pain reduction 4 hours after the injection were 3.38 times as likely to be responders as those experiencing ≤50% pain reduction (OR 3.38, 95%CI 1.07-10.65). The effect decreased between day 1-2, but re-appeared on day 3 and was strongest on day 6 (OR 6.87, 95%CI 1.99-23.72). It remained significant until day 14.

Conclusions

The results of this study can guide physicians in managing patients with lumbar disc herniations: A <50% leg pain relief within 1 week after a transforaminal epidural steroid injection predicts an unfavorable 1-month outcome and suggests that other treatment options may be considered at an earlier point in time.

028

Heart rate variability in REM sleep has properties of a biomarker for major depression

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Objectives

Heart rate variability (HRV) is known to be an indicator of the activity of the autonomous nervous system (ANS) having properties of a biomarker indexing stress related diseases. However, HRV studies commonly focus on wake time processes and provide only small effect sizes. Therefore, our aim was to investigate in HRV in sleep and in its properties as biomarker for affective disorders. Our hypotheses were, that (1) HRV separates between sleep stages, (2) that HRV in rapid eye movement (REM)sleep separates between healthy and depressed subjects without antidepressant (AD) medication, and (3) that HRV differs between responders and non-responders of AD-Treatment.

Methods

To examine hypothesis (1) and (2) we assessed twenty-one young, depressed out-patients without AD-treatment (age: 24 ± 3 y; 52% females) and a healthy control group. To examine, if HRV would predict response to AD-treatment, we assessed another sample of thirty-three depressed in-patients under AD-treatment, at week one and at week four (age: 46 ± 16 y, 64% females), and, again, compared these patients to a healthy control group. All participants were examined in a sleep laboratory. HRV measures were derived from pure REM, N2 and N3 sleep periods, resp. Treatment response at week four was defined as $\leq 50\%$ reduction of baseline Hamilton Depression score.

Results

HRV frequency domain measures differed significantly between N2, N3 and REM sleep with high VLF power, intermediate LF power, and low HF power in REM sleep and reciprocal results in N3 sleep. In the young out-patients we found lower relative HF and higher relative VLF power in REM sleep compared to healthy subjects, each with large effect sizes (Cohen's $d = 0.9$), and similar results in the treated in-patients. In the in-patients HRV-measures at week one did not predict response or non-response to antidepressants at week four. Moreover, over the time of treatment decreased HF power in REM sleep did not change despite psychopathological improvement.

Conclusions

Sleep-EEG stages were reflected by HRV measures distinctly. In two independent controlled studies HRV in REM sleep separated between healthy subjects and patients with large effect sizes. The observation that decreased HF power in REM sleep did not change along with clinical improvement indicated that HRV in REM sleep may be a trait marker of depression.

029

Influence of adjuvant metacognitive detached mindfulness and stress management training compared to pharmacologic treatment in primiparae with postpartum depression

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Ten to 15% of mothers experience postpartum depression (PPD). If untreated, PPD may negatively affect mothers' and infants' mental health in the long-term. Accordingly, effective treatments are required. In the present study we investigated the effect of metacognitive detached mindfulness (MDM) and stress management training (SMT) as adjuvants, compared to pharmacologic treatment only, on symptoms of depression in women with PPD. 45 primiparae (mean age: $M=24.5$ years) with diagnosed PPD and treated with an SSRI (citalopram; CIT) took part in the study. At baseline, they completed questionnaires covering socio-demographic data and symptoms of depression. Experts rated also symptoms of depression. Next, participants were randomly assigned to one of the following study conditions: adjuvant metacognitive detached mindfulness (CIT+MDM); adjuvant stress management training (CIT+SMT); control condition (CIT). Self- and experts' ratings were completed at the end of the study eight weeks later, and again at eight weeks follow-up. Symptoms of depression decreased significantly over time, but more so in the CIT+MDM and CIT+SMT group, compared to the control condition. The pattern of results remained stable at follow-up. In primiparae with PPD and treated with a standard SSRI, adjuvant psychotherapeutic interventions led to significant and longer-lasting improvements.

O30**The origins of mental toughness – prosocial behavior, and low internalizing and externalizing problems at the age of 5 years predict higher mental toughness scores at the age of 14 years**

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Background

The concept of mental toughness has gained increasing importance among non-elite athletes for its psychological importance and explanatory power for a broad range of health-related behaviors. On the flip side, no study has focused so far on the psychological origins of mental toughness. Therefore, the aims of the present study were three-fold: To explore, to what extent psychological profiles of preschoolers at the age of five years predicted mental toughness scores and sleep disturbances at the age of 14 years, and to explore possible gender differences.

Method

Nine years after their first assessment at the age of five years (preschoolers), a total of 77 adolescents (mean age: 14.35 years; SD = 1.22; 42% females) took part in the present follow-up study. At baseline, both parents and teachers completed the Strengths and Difficulties Questionnaire (SDQ), covering internalizing and externalizing problems, hyperactivity, negative peer relationships, and prosocial behavior. At follow-up, participants completed a booklet of questionnaires covering socio-demographic data, mental toughness, and sleep disturbances

Results

Preschoolers with high prosocial behavior and low internalizing and externalizing problems, as rated by parents and teachers, at the age of 14 years self-reported higher mental toughness and lower sleep disturbances. At the age of 14 years, and relative to their male counterparts, female participants reported lower MT scores and higher sleep disturbances.

Conclusions

The pattern of results suggests that mental toughness traits during adolescence have their origins during pre-school years.

031

Single intravenous injection of ketamine : antidepressant and adverse effects

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Introduction

Ketamine, an approved anaesthetic agent modulating glutamatergic neurotransmission, is studied as a novel approach to treat depression. Almost all approved antidepressants target monoaminergic neurotransmission and have a delayed onset of clinical effects.

Method

We included 10 severely depressed patients and administered them a unique dose of ketamine intravenously (0.5mg/kg of weight, administration during 1 minute). Patients had to be resistant to pharmacotherapy, and to have a stable psychotropic medication. They were not allowed to suffer from psychiatric comorbidities others than anxiety disorders and nicotine addiction and did not have any contra-indication to the administration of ketamine. The severity of depression was assessed with the MADRS, the HAM-D scale and the BDI.

Results

Median MADRS score at baseline was 29 (range 26-34). Nine patients finished the whole study protocol, including a 4-week post-injection observation period. One patient had to be excluded after 1 week, due to increased suicidality. This was the only severe adverse event recorded. As measured by the MADRS, depression scores were significantly lower than baseline between 40 min and 15 days after ketamine administration ($p < 0.05$). Most frequent side effects directly linked to ketamine administration were mild to moderate and transient hypertension (10 patients, systolic/diastolic blood pressure $> 140/90$ mm HG) and somnolence (6 patients).

Discussion

This is one of a very small number of studies assessing the antidepressant effects of ketamine in which the intravenous administration was relatively short (1 min vs. 45 mins in most other studies). The antidepressant effect occurred very rapidly after the injection, and was sustained. Adverse effects were mild to moderate, with only one severe adverse event, which could not be directly attributed to the administration of ketamine, but to the underlying illness. To our knowledge, no dose-finding study with ketamine has yet been published, and the relatively sustained antidepressant effect in our study could be linked to the use of a fast drug infusion scheme.

032

Impairment of recollection memory following selective lesion of the fornix: insights from functional Magnetic Resonance Imaging.

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Hippocampal lesions have dramatic effects on memory abilities. Previous studies collectively suggest that associative memory crucially depends on hippocampal integrity. However, other circuits connected to the hippocampus, such as the fornix, may have similar effects. Previous behavioural work in animals and humans indeed suggest that lesion of these fibers selectively impairs recollection compared with familiarity-based recognition. We studied associative memory abilities in a patient with selective damage of the fornix using functional MRI. The patient (female, right-handed, 64 years old, 12 education years) suffered from a selective damage of bilateral fornix (ischemic stroke). Deficits in anterograde and retrograde episodic memory persisted at 4 months. We used a simple visual associative memory test. At encoding, pictures pairs were semantically related or not, to test for semantic memory. At recognition, a target was presented with 2 items: the previously associated object and a distracter, which is either a new or old object (paired with another item at encoding), to assess Familiarity-based (FAM) vs. Recollection-based (REC) memory respectively. The control group was composed of 6 healthy women (right-handed, 65.5 ± 4.5 years old, 11.8 ± 0.4 education years). Brain activity and T1-weighted anatomical data were collected using MRI (3T). Brain activity in controls and the patient were compared using two tailed t-tests ($p < 0.005$ uncorrected) with the SPM toolbox. The patient performed as well as controls in FAM trials, but made more errors than controls in the REC condition ($p < 0.05$). At encoding, while the patient recruited an additional parieto-occipital network compared to controls, the controls showed additional recruitment of a temporal network (bilateral inferior temporal gyrus, medial temporal pole). At recognition and in REC trials, only frontal orbital areas and the posterior parietal cortex were more activated in the patient vs. controls. In contrast, a typical network of occipito-temporal and medial parietal area was more recruited in controls vs. patient ($p < 0.005$). Again for FAM trials, the frontal orbital area was more activated in the patient, while controls showed mainly more activity in the occipito-temporal areas. The data indicate that a selective damage of the fornix can 1) alter associative memory already at encoding, and 2) impair Recollection-based recognition but 3) spare Familiarity-based recognition with compensatory processes.

O33**Investigating the role of Dgcr2 on cortical projection neuron development**

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Alterations in early steps of cortical circuit formation are thought to play an important role in vulnerability to schizophrenia (SZ). DiGeorge Critical Region 2 (Dgcr2) is located in the 22q11.2 locus, whose deletion is one of the highest known risk factor for SZ, and codes for an activity-dependent trans-membrane protein expressed during cortical development. In addition, exome sequencing revealed a de novo Dgcr2 missense mutation in an idiopathic schizophrenic patient. The present study intends to understand the function of Dgcr2 in pyramidal neurons migration and in cortical circuit formation. Here we investigated the expression and function of Dgcr2 in early steps of cortical circuit formation using in utero electroporation targeted to projection neurons (PNs). Knock-down (kd) of the expression of mouse (m)Dgcr2 during corticogenesis affected the laminar positioning of PNs in a persistent manner in the somatosensory cortex and the medial prefrontal cortex. PN mispositioning due to Dgcr2 kd could be fully rescued by overexpressing the human (h)DGCR2 but not the (h)DGCR2 containing the SZ-risk mutation, indicating a deleterious impact of this SZ-risk mutation on PNs migration. In order to further understand the biological function of Dgcr2, we are currently investigating the role of specific DGCR2 subdomains and studying potential binding partners. This study will bring novel insights on the role of the SZ-risk gene Dgcr2 on cortical circuit assembly.

034

Neuronal ganglia as a cause of peripheral nerve lesion - clinical and neurosonographic findings

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Introduction

Clinical and electrophysiological examination is the standard of care for patients with peripheral nerve lesions. Recently, high resolution dynamic ultrasound has emerged as a novel diagnostic tool in the management of peripheral nerve lesions. Occasionally, neuronal ganglia have been identified as the underlying cause of nerve damage. We report our findings of extra- and intraneural ganglia detected by neurosonography.

Methods

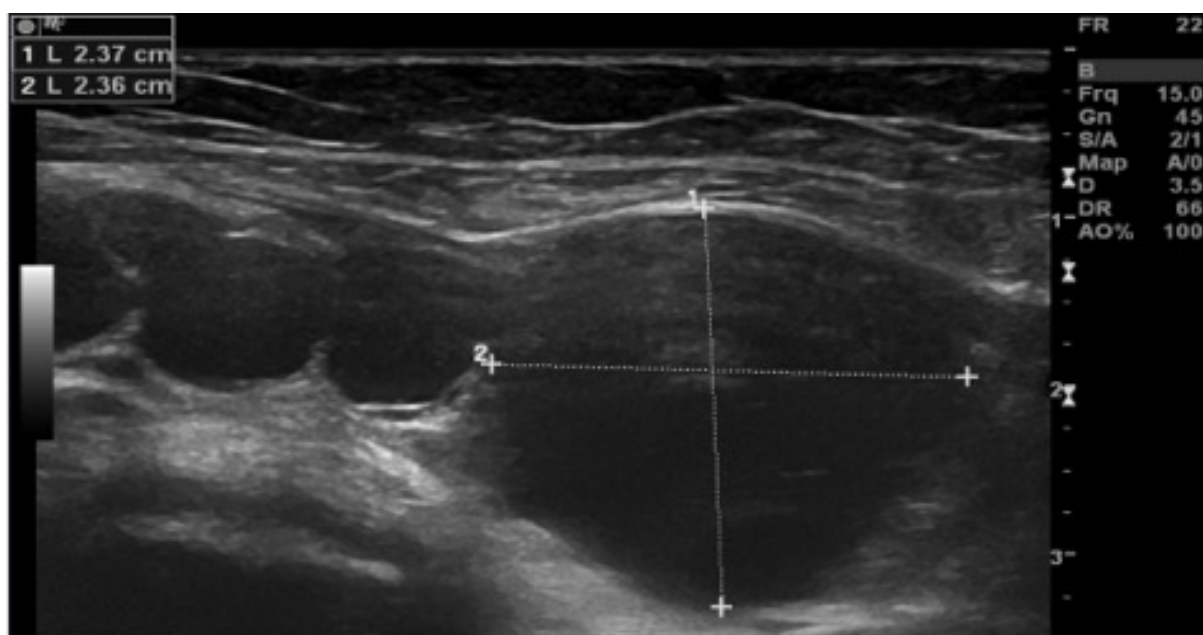
As a large referral hospital in eastern Switzerland we reviewed our institutional database for patients with nerve ganglia as the cause for peripheral nerve lesions who underwent sonographic evaluation (18 MHz linear array transducer, Philipps Epic Q5).

Results

In an unselected cohort of patients referred to nerve sonography within the last 3 years we identified 9 out of 471 patients (1.9%) with intraneural (n=5) and extraneural (n=4) ganglia of various nerves (1 combined tibial and peroneal, 1 tibial, 3 common peroneal, 2 deep peroneal, 1 tibial in tarsal tunnel, 1 radial). 7 out of 9 patients presented with painful sensorimotor nerve palsies, 2 with painless symptoms. Except for one patient all underwent surgical resection with intermediate to slow improvement of peripheral nerve function. One asymptomatic relapse of an extraneural peroneal ganglion was detected only by nerve sonography.

Discussion

High-resolution dynamic nerve ultrasound is a useful tool in the clinical management of peripheral nerve lesions, especially in atypical case presentations like painful nerve palsies. Extraneural and intraneural ganglia of the extremities are easily detected by this method. Despite being rare in an unselected patient cohort, detection of nerve ganglia dramatically changes therapeutic strategies with need of surgical decompression and ligation of the articular branch to prevent relapses. Sensitivity and specificity of sonographic findings are strongly guided by clinical and electrophysiological evaluation. In our understanding nerve sonography is an addition to the neurological diagnostic work-up and not a stand-alone technique.



O35

Epilog: Framework for automatic, standardized EEG source imaging to localize the epileptogenic zone

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Purpose

The purpose of the study is to investigate the value of automatic detection of interictal epileptiform discharges and subsequent EEG source imaging (ESI) to localize the epileptogenic zone during the presurgical evaluation of epilepsy patients.

Method

In this study 35 patients who underwent a complete pre-surgical work-up followed by resective surgery were included. Twenty-four and 11 patients had long term EEG monitoring recorded with the standard clinical set-up in Ghent University Hospital, Belgium and in Geneva University Hospital, Switzerland, respectively. Patient details are shown in table 1. Epileptic spike detection was performed using Persyst P13. Afterwards the 3 most prominent spike clusters were localized using in-house ESI. For this, a 6-layer patient-specific head model including gray matter, white matter, cerebrospinal fluid, skull, scalp and air, was constructed from the MRI and sLORETA was used to localize the spikes in the brain. The distance to the border of the resection was calculated. Sensitivity and specificity of the proposed method to identify the epileptogenic focus were assessed. The complete Epilog pipeline is imaged in fig.1.

Results

The median and mean distances to the resection and the sensitivity and specificity of the proposed pipeline are shown in table 2. The mean and median distances were lower in seizure-free compared to non-seizure-free patients. The most prominent spike cluster had the lowest distance to resection. The individual distances are shown in fig. 2. The localization of the spike cluster with most occurrences had a sensitivity of 71% and specificity of 75% to localize the EZ. This sensitivity increased to 81% and specificity stayed equal to 75% when the second most prominent cluster was included. Incorporating the third most prominent cluster led to an increased sensitivity of 87% and a decreased specificity of 50%. Discussion: The automatic detection of spikes in long term clinical EEG recordings followed by ESI has a higher sensitivity and specificity than more established techniques in the pre-surgical evaluation such as ictal SPECT (sens 58% and spec 47%), interictal PET (sens 68% and spec 44%) or structural MRI (sens 76% and spec 53%).

Conclusion

We showed that ESI of automatically detected spikes is a non-invasive technique with high sensitivity and specificity that deserves a more prominent role during the presurgical evaluation of epilepsy.

Table 1

PAT ID	SF	University Hospital	EEG duration (hh:mm:ss)	# detected spikes			Surgery type	Resection volume	Distance to resection		
				cluster1	cluster2	cluster3			cluster 1	cluster 2	cluster 3
1	1	Gent	60:00:02	208	124	113	right anterior 2/3 temporal lobectomy incl. hippocampectomy	6.84	38	33	34
2	1	Gent	53:55:44	97	11	8	temporal left lesionectomy	21.45	0	4	41
3	1	Gent	63:00:38	17730	1204	60	left temporal lobectomy with additional left temporobasal topectomy	5.86	1	5	1
4	1	Gent	83:13:12	616	469	300	selective right amygdalohippocampectomy	6.30	1	0	32
5	1	Gent	57:00:37	2344	284	214	selective left amygdalohippocampectomy	21.23	0	0	45
6	1	Gent	39:00:02	1191	250	61	right frontal and opercular topectomy/lesionectomy	1.18	49	49	39
7	1	Gent	83:13:12	1905	1210	287	selective right amygdalohippocampectomy	1.30	36	49	70
8	1	Gent	77:13:10	7512	5247	88	selective right amygdalohippocampectomy	1.94	1	0	4
9	1	Gent	83:13:12	5857	1890	360	resection of cavernoma subinsular right and surrounding epileptogenic tissue	14.56	17	20	27
10	1	Gent	83:13:12	813	465	403	selective right amygdalohippocampectomy	3.25	50	64	77
11	1	Gent	21:44:00	2238	850	472	right temporal topectomy and amygdalohippocampectomy	4.69	10	35	1
12	0	Gent	72:49:03	1809	770	537	microsurgical resection of epidermoidcyst mesiotemporal left and prefrontal	41.34	35	41	16
13	1	Gent	83:13:12	5064	640	535	right temporobasal for resection of epileptogenic lesion	4.76	0	2	1
14	1	Gent	26:31:59	279	160	73	selective right amygdalohippocampectomy	48.31	0	0	66
15	0	Gent	24:20:15	2295	835	239	partial right anterolateral temporal lobectomy	2.64	22	22	75
16	1	Gent	00:33:17	2	1	0	left occipital laisionectomy (ganglioglioma WHO grade II and epileptogenic zone anterior)	34.65	0	37	NA
17	1	Gent	16:35:15	130	44	40	selective left amygdalohippocampectomy	3.59	33	15	34
18	1	Gent	41:31:59	267	76	24	left anterior temporal lobectomy, incl.	6.71	7	7	51
19	1	Gent	08:26:15	8	7	6	amygdalohippocampectomy and laisionectomy	5.91	8	49	27
20	1	Gent	24:06:04	5108	3021	92	selective right amygdalohippocampectomy	3.84	30	15	58
21	1	Gent	90:50:28	46617	38189	2482	extended corticectomy left frontal, temporal and insular	14.02	5	5	0
22	1	Gent	62:10:54	5296	2908	1679	resection of brain tumor (astrocytoma WHO grade II) left mesio-occipital and hippocampal	13.09	20	39	40
23	1	Gent	01:29:35	87	21	4	selective left amygdalohippocampectomy	4.17	1	0	13
24	0	Gent	102:00:03	55801	38529	35506	perilaeisonal topectomy left frontal	71.59	9	21	9
25	0	Geneve	08:54:27	352	46	21	Left Parietal parasagittal corticectomy	37.95	65	43	45
26	1	Geneve	01:55:43	221	20	14	Right Anterior Temporal Lobe Resection	38.96	7	28	80
27	1	Geneve	04:53:06	1129	242	51	Tuber resection Left Frontal anterior, Left Central	50.86	39	16	44
28	1	Geneve	03:11:39	118	38	15	Right Frontal topectomy	36.70	21	40	14
29	1	Geneve	04:41:52	1624	226	127	Left Parietal lesionectomy	6.27	17	21	21
30	1	Geneve	05:39:36	905	419	141	Left Anterior Temporal Lobe Resection sparing mesial Temporal structures	44.96	12	5	38
31	0	Geneve	08:25:40	2414	346	156	Right Temporal and Right Parietal lobectomy	25.19	59	47	17
32	1	Geneve	03:49:29	6733	1516	770	Left Temporal lobectomy	34.18	8	14	27
33	1	Geneve	12:37:08	355	269	241	Right amygdalo-hippocampectomy	5.49	16	52	40
34	1	Geneve	03:41:01	656	394	57	Left amygdalo-hippocampectomy	8.73	8	79	35
35	1	Geneve	07:30:34	3711	348	82	Left Anterior Temporal Lobe Resection	12.60	1	0	27

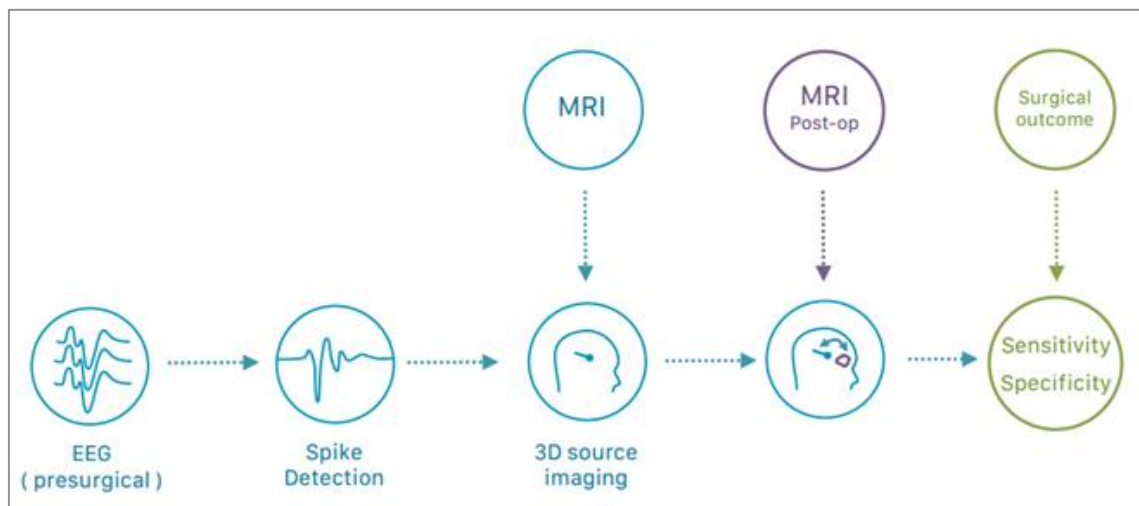


Fig 1

Table 2

	clus1	clus2	clus3	clus1+2	clus1+2+3
median distance SF	8.12	15.54	34.5	13.19	19.75
mean distance SF	17.92	24.34	33.11	21.13	25.12
median distance NSF	11.92	6.63	34.1	9.46	14.57
mean distance NSF	19.57	17.27	28.21	18.42	21.68
sensitivity	73%	57%	23%	83%	87%
specificity	80%	100%	40%	80%	40%

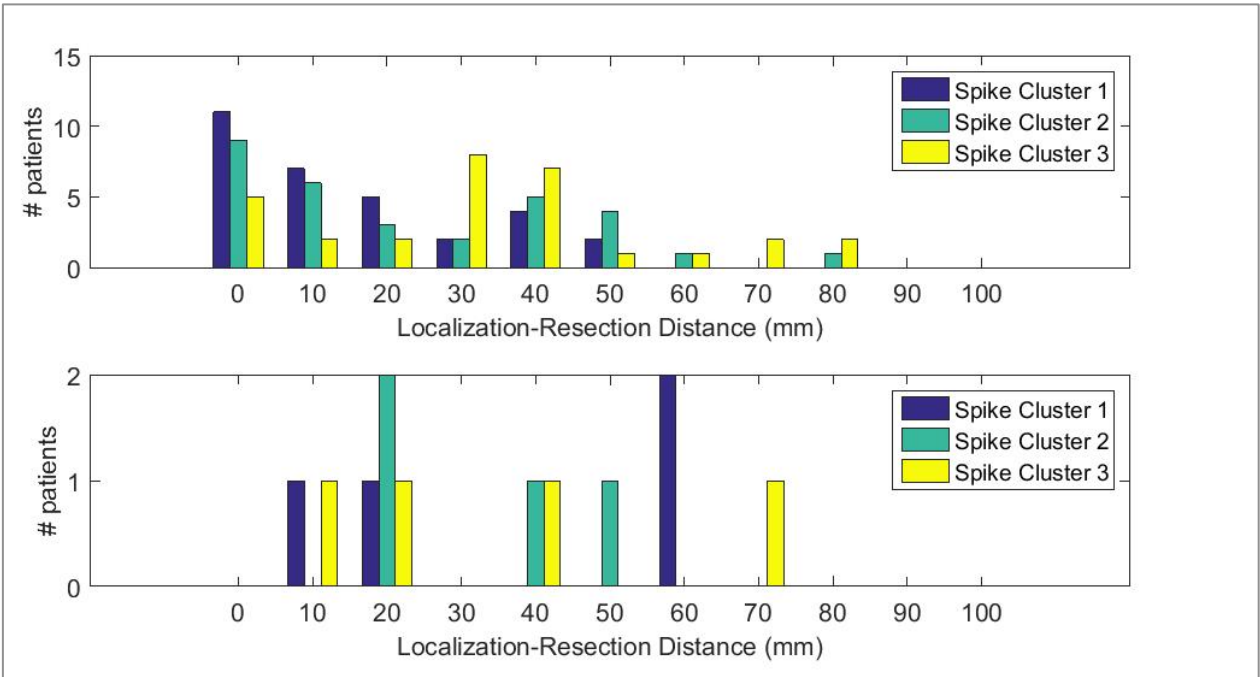


Fig. 2

036

Postictal testing can predict post-operative verbal memory decline in pharmacoresistant temporal lobe epilepsy patients

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Background

Temporal lobe epilepsy (TLE) is the most frequent form of pharmacoresistant epilepsy. Up to 84% of the patients benefitting from epilepsy surgery can become seizure free. One of the feared complications of TLE surgery is a decline of episodic verbal memory. Our study evaluates the predictive value of postictal verbal memory testing in predicting the post-operative verbal memory decline.

Methods

We have retrospectively analyzed the electronic health records and neuropsychological examination files of patients who underwent unilateral resection of medial temporal lobe structures in our university hospital between 10/1995–11/2011. Seventy-four consecutive patients (50% male, age 12-57, mean 31.3 years) had a neuropsychological evaluation carried out in interictal, postictal and post-operative periods. Rey auditory-verbal learning task and Rey visual design standardized tests of 15 items each were used for memory assessment. We estimated the predictive value of postictal verbal delayed recall (VDR) to predict the post-operative VDR. The same analysis was then performed in the subgroup of patients with hippocampal sclerosis (HS).

Results

The mean follow up time was 11.3 months (range 3-46). Thirty-one (46.3%) patient had at least 1 item decrease in the post-operative VDR. Nineteen (28.4%) patients had a clinically significant decline of 20% (3 items) of VDR. The left TLE patients had more pronounced postictal VDR decline (20.1 vs. 16.1%, $p=0.04$), lower scores in VDR at 3 months (59.0 vs. 78.6%, $p<0.001$) and 12 months (53.5 vs. 79.0%, $p=0.015$) after surgery. The interictal VDR score correlated negatively with the post-operative VDR decline ($CC = -0.415$, $p<0.001$). The 40% postictal VDR decline was the optimal cut-off to predict a 20% post-operative VDR decline in the whole test group and the HS ($n=49$) group (sensitivity = 0.389, specificity = 0.867, AUC 0.628 and sensitivity 0.455, specificity 0.900, AUC 0.677 respectively).

Conclusions

Our findings are concordant with the theory that functional hippocampal adequacy contributes to the post-operative verbal memory decline, i.e. the better the memory before the operation, the more function there is to lose. This is the first study to estimate the prediction of postictal testing at different cut-off thresholds. The presence of 40% postictal verbal delayed recall clearly increases the risk of clinically significant post-operative verbal memory decline.

037

A novel suppression head impulse paradigm (SHIMP) elicits anti-compensatory saccades as an indicator of vestibular function

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038

Quality control of Motor Unit Number Index (MUNIX) in 6 muscles in a single-subject "Round-Robin"

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Background

Reliability of biomarker measurements is paramount to their successful implementation into clinical trials. Motor Unit Number Index (MUNIX) is a neurophysiological measure that provides an index of the number of lower motor neurons supplying a muscle. Its performance across centres in healthy subjects and patients with Amyotrophic Lateral Sclerosis (ALS) has been established, but inter-rater variability between multiple raters from different centres in one single subject, comparable to a round robin test in laboratory medicine, has not been investigated.

Objective

To assess intra- and inter-rater variability in a set of 6 muscles in a single subject among 12 examiners (6 experienced with MUNIX, 6 less experienced) and to determine variables associated with variability of measurements.

Methods

Neurologists and neurophysiologist from 12 European ALS centres applied MUNIX in six different muscles (abductor pollicis brevis (APB), abductor digiti minimi (ADM), biceps brachii (BB), tibialis anterior (TA), extensor dig. brevis (EDB), abductor hallucis (AH)) twice in one single volunteer on consecutive days. All raters had attended at least one training course prior to measurements. Intra- and inter-rater variability as determined by the coefficient of variation (COV) between different raters and their levels of experience with MUNIX were compared.

Results

Mean intra-rater COV of MUNIX was 14.0% (± 6.4) ranging from 5.8 (APB) to 30.3% (EDB). Mean inter-rater COV was 18.1 (± 5.4) ranging from 8.0 (BB) to 31.7 (AH). No significant differences of variability between experienced and less experienced raters were detected.

Conclusion

We provide evidence that quality control for neurophysiological methods can be performed with similar standards as in laboratory medicine. Intra- and inter-rater variability of MUNIX is muscle-dependent and mainly below 20%. Experienced neurophysiologists can easily adopt MUNIX and adequate teaching ensures reliable utilization of this method.

039

Disease-specific sparing of the anterior semicircular canals in bilateral vestibulopathy

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Objective

Bilateral vestibular loss (BVL) is often diagnosed with great delay and an underlying cause is only identified in 50-80%. We measured horizontal and vertical semicircular canal function using the video-head-impulse test (vHIT) and hypothesized that specific vHIT-patterns may be linked to certain etiologies.

Methods

We retrospectively analyzed 109 BVL-patients linked to aminoglycoside vestibulotoxicity (n=16), Menière's disease (n=10), infectious inner-ear disorders (n=11), sensorineural hearing-loss (n=11), cerebellar-ataxia-neuropathy-vestibular-areflexia-syndrome (CANVAS, n=5), other causes (n=19) as well as those with unknown origin (n=47). Vestibulo-ocular reflex gains and cumulative saccade amplitudes were measured with vHIT, and the functional integrity of all semicircular canals was rated.

Results

Overall, anterior canal hypofunction (n=86/218) was identified significantly ($p < 0.001$) less often than horizontal (n=186/218) and posterior (n=194/218) hypofunction. Preserved anterior canal function was associated with aminoglycoside vestibulotoxicity, Menière's disease and BVL of unknown origin, while no such sparing was found for inner-ear infections, CANVAS and sensorineural hearing loss.

Conclusions

Semicircular canal function in BVL shows disease-specific dissociations, potentially related to reduced vulnerability or superior recovery of the anterior canals.

Significance

In patients with suspected BVL we recommend quantifying vHIT gains and saccade amplitudes for all semicircular canals as the pattern of canal hypofunction may help identifying the underlying disorder.

040

Ocular vestibular evoked myogenic potentials as a test for myasthenia gravis

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O41

Ocrelizumab No Evidence of Disease Activity (NEDA) Status at 96 Weeks in Patients With Relapsing Multiple Sclerosis: Analysis of the Phase III Double-blind, Double-dummy, Interferon Beta-1a-controlled OPERA I and OPERA II Studies

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Objective

To evaluate the effect of ocrelizumab vs interferon beta-1a (IFN β -1a) on achieving no evidence of disease activity (NEDA) in patients with relapsing MS over 96 weeks in two identical Phase III, randomized, double-blind, double-dummy trials (OPERA I and OPERA II).

Background

MS treatment goals are evolving with the emergence of higher-efficacy therapies. NEDA is a composite measure of the absence of clinical and MRI findings and a rapidly-emerging treatment goal.

Methods

In OPERA I and OPERA II, patients were randomized (1:1) to receive ocrelizumab 600mg via intravenous infusion every 24 weeks or subcutaneous IFN β -1a 44 μ g three times weekly over 96 weeks. NEDA (defined as no relapses, confirmed disability progression [CDP], new/enlarging T2 lesions or gadolinium-enhancing T1 lesions) was analyzed over 96 weeks. MRI was assessed at baseline, 24, 48, and 96 weeks.

Results

At 96 weeks, 47.9% and 47.5% of ocrelizumab-treated patients vs 29.2% and 25.1% of IFN β -1a-treated patients achieved NEDA in OPERA I (64% increase; $p < 0.0001$) and OPERA II (89% increase; $p < 0.001$), respectively; 80.4% and 78.9% of ocrelizumab-treated patients vs 66.7% and 64.5% of IFN β -1a-treated were without relapses; 92.4% and 89.4% of ocrelizumab-treated patients vs 87.8% and 84.9% of IFN β -1a-treated were without CDP; 91.7% and 90.2% of ocrelizumab-treated patients vs 69.8% and 63.9% of IFN β -1a-treated were without gadolinium-enhancing T1 lesions; and 61.7% and 60.9% of ocrelizumab-treated patients vs 38.7% and 38.0% of IFN β -1a-treated were without new/enlarging T2 lesions in OPERA I and OPERA II, respectively. After week 24, $\geq 96.0\%$ of all ocrelizumab-treated patients were without new/enlarging T2 lesions.

Conclusions

Ocrelizumab consistently resulted in greater achievement of NEDA vs IFN β -1a over 96 weeks, with elimination of new/enlarging T2 lesions in nearly all patients after week 24. Delaying baseline NEDA analysis until after therapy initiation may more accurately reflect the therapeutic potential of an agent. Supported by F. Hoffmann-La Roche Ltd.

042

Unilateral ablation of the cerebellothalamic tract in essential tremor by MRI-guided high intensity focused ultrasound

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Background

MRI-guided high intensity focused ultrasound (MRigFUS) allows for the selective ablation of deep brain structures under direct MRI guidance. As the main cerebellar afferent to the thalamic ventral intermedius nucleus, the cerebellothalamic tract is part of the pathophysiological network in essential tremor (ET). We report results of a prospective trial of unilateral transcranial MRgFUS ablation of the cerebellothalamic tract in ET.

Methods

Prospective, uncontrolled, open-label, blind-assessed, single center interventional study (clinicaltrials.gov identifier: NCT01698450). ET patients fulfilling criteria for interventional therapy received unilateral ablation of the cerebellothalamic tract by MRigFUS (ExAblate Neuro MRigFUS system). Motor, manual dexterity, cognitive and quality of life examinations were assessed pre-, 48h and 1, 3 & 6 months post intervention. Standardized video-recordings were rated and tremor sub-scores calculated by movement disorder neurologists not involved in the treatment. Primary outcome was the change in unilateral hand tremor score of the treated hand (items 5, 6, 11-14 of the Clinical Rating Scale for Tremor (CRST)) between baseline and 6 month follow-up).

Findings

6 patients received MRigFUS ablation of the cerebellothalamic tract contralateral to the treated hand. Repeated measures comparison determined a statistically significant reduction (pre – 6 month post intervention mean $\pm$ SD; absolute reduction; 95% CI) in the unilateral treated hand sub-score (14.3 ± 4.9 vs. 2.5 ± 2.6 ; -11.8 , 95% CI 8.4 to 15.2 ; $p < 0.001$), while there was no change in the non-treated hand. Measures for manual dexterity, attention & coordination and overall cognition were unchanged. Transient side effects ($n=3$) were ipsilateral hand clumsiness and mild gait instability for up to maximal 3 months.

Interpretation

Unilateral MRigFUS lesioning of the cerebellothalamic tract was highly efficacious in reducing contralateral hand tremor in ET. Adverse effects were mild and transient.

Funding

This investigator-initiated trial received no funding.

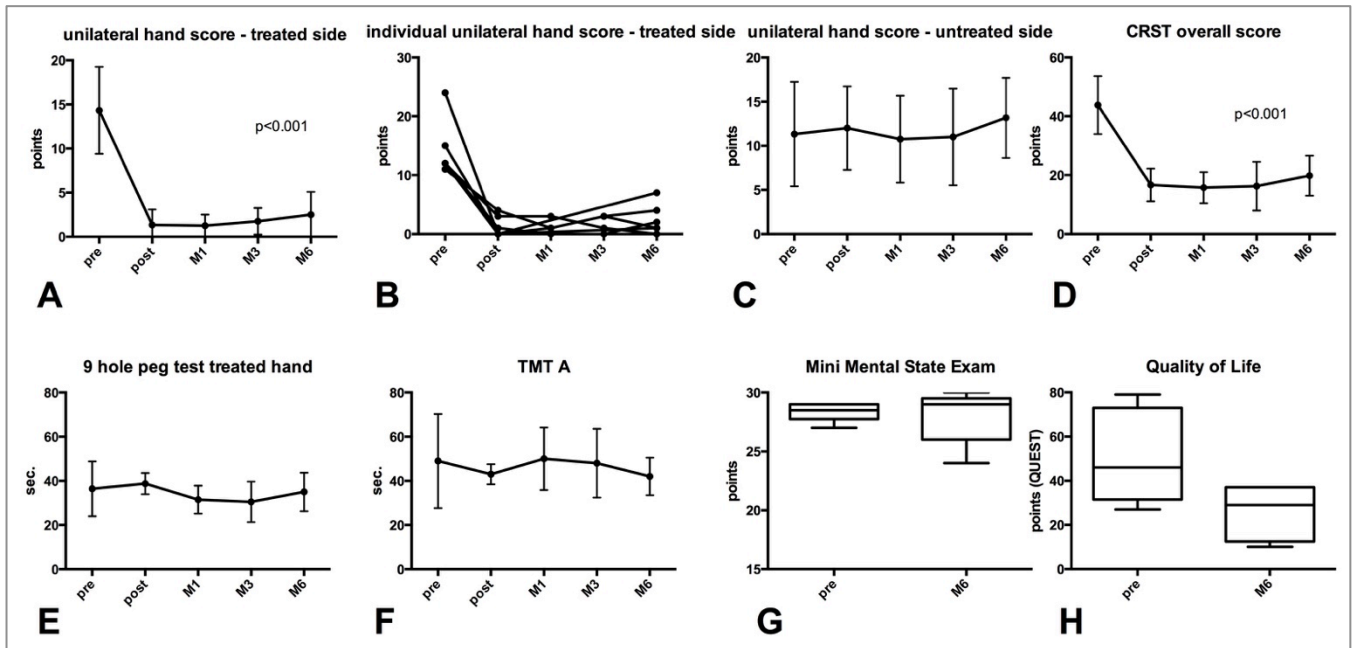


Figure: Six-month follow-up results of unilateral CTT MRgFUS lesion on CRST tremor scores of the treated (A, B) and untreated hand (C) and overall tremor severity (D), manual dexterity (E), fine motor tasks (F), cognition (G) and quality of life (H) in advanced ET patients.

043

Lower relapse rates with natalizumab as compared with fingolimod as second-line treatment in relapsing-remitting multiple sclerosis

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Background

Placebo controlled phase III trials have shown superiority of fingolimod and natalizumab on clinical and MRI two year outcomes. No randomized controlled trial compared fingolimod and natalizumab in relapsing-remitting(RRMS) directly.

Objective

To compare clinical outcomes in patients with RRMS receiving fingolimod or natalizumab as second line disease modifying treatment (DMT) in a large observational study in Switzerland.

Methods

Data were derived from the Swiss Federation for Common Tasks of Health Insurances that controls reimbursement of DMT prescription in Switzerland. Inclusion criteria were: RRMS, switch to fingolimod or natalizumab after DMT with Interferon Beta or Glatiramer acetate for at least one year and one or more relapses in the year prior to switch. Patients treated with fingolimod or natalizumab were 1:1 propensity score matched using age, gender, disease duration, Expanded Disability Status Scale(EDSS), relapses in the previous year, time to last relapse, as baseline matching characteristics. Quality matching was assessed using the analysis of standardized differences. Cumulative incidence of relapse and one-year confirmed disability progression was calculated using Kaplan-Meier estimates. The hazard of disease progression and relapse was compared using Cox-proportional hazards models. Patients who discontinued or switched DMT were censored

Results

In total, 438 patients were included: 219 fingolimod vs. 219 natalizumab treated; 74.4% were female, mean age 38.2 ± 10.2 and disease duration 7.7 ± 6.6 years, median EDSS 3.0(IQR 2.0-3.5), number of relapses in the previous year 2.0 ± 2.3 . Proportions of relapse-free patients on fingolimod and natalizumab were 76% vs. 88% after 1 year, 64% vs. 83% after 2 years and 60% vs. 78% after 3 years, respectively with a 50% reduction in relapse hazard(HR: 0.50; 95% CI: 0.34-0.73; $p < 0.001$). EDSS data were complete in 132 patients with natalizumab and 132 patients with fingolimod. The cumulative proportions of patients with EDSS progression on fingolimod vs. natalizumab were 2.3% vs. 4.2% after 1 year, 7.1% vs. 10.8% after 2 years, 10.7% vs. 17.6% after 3 years, respectively. Time to one-year confirmed EDSS progression was similar in both treatment groups(HR: 1.49; 95% 0.68-3.28; $p=0.324$).

Conclusions

In clinically active RRMS switch from platform DMT to natalizumab was associated with lower relapse-rates vs fingolimod over 3 years. No differences were observed with regard to disability.

O44

Resting-state fMRI properties of inhibition abilities in healthy children and young adults

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Aim

Inhibition, as part of executive functions, develops throughout childhood. The right inferior prefrontal gyrus (rIFG) is known to play a crucial role in inhibition and attention control in adults. Little is known about resting-state properties associated with inhibition in healthy children. We therefore investigated resting-state functional imaging (rsfMRI) in correlation with inhibition in a cohort of healthy children and young adults.

Methods

High-resolution T1-weighted MR structural images and rsfMRI (simultaneous multi-slice technique with TR=300ms, multiband factor 8) were performed. Conn toolbox 13.1 was used to explore resting-state features of pre-defined regions of interest (ROI). The method was first tested in a pre-analysis by correlating the right primary motor cortex (rPMC) with grip-strength (max. value of 3 trials in dominant hand), as investigating motor features was expected to be robust. As a measure of inhibition, the scaled score (SS) of the amount of errors during a Color-Word-Interference task (CWI; D-KEFS) was selected. The rIFG was chosen as ROI. A general linear model was used to examine rsfMRI properties of the rIFG and inhibition (age adjusted; $p=.05$, FDR corrected).

Results

25 healthy participants were included (20 females; age range: 6.1-25.1, mean: 16.2). Mean group performance during the CWI task was normal (SS time: 11.44 (SD 1.89); SS errors: 9.36 (SD 2.58)). Examination of grip-strength (mean: 12.5 pound-force per square inch, SD=4.01) and the rPMC revealed a positive connection to the left PMC (lPMC; $p<.05$). Examination of inhibition and the rIFG revealed significantly negative connections to the left and right primary visual (lPVC, $p=.03$; rPVC, $p=.02$) and right secondary visual cortices (rSVC, $p=.02$) (Figure 1).

Discussion

The finding of the pre-analysis (the stronger the connectivity between rPMC and lPMC, the higher the grip-strength of participants) seems appropriate. Hence, the reliability of the method is assumed to be given. As the PVC and SVC are involved in visuo-spatial information processing, we assume that inhibition processes in the rIFG might be less disturbed when connectivity between rIFG and VC is reduced, as interference by task-irrelevant visual stimuli is less likely. We suggest that the more the rIFG-VC connectivity is being suppressed in children, the better their inhibition. The findings could provide normative data for further analyses including children with neurological deficits.

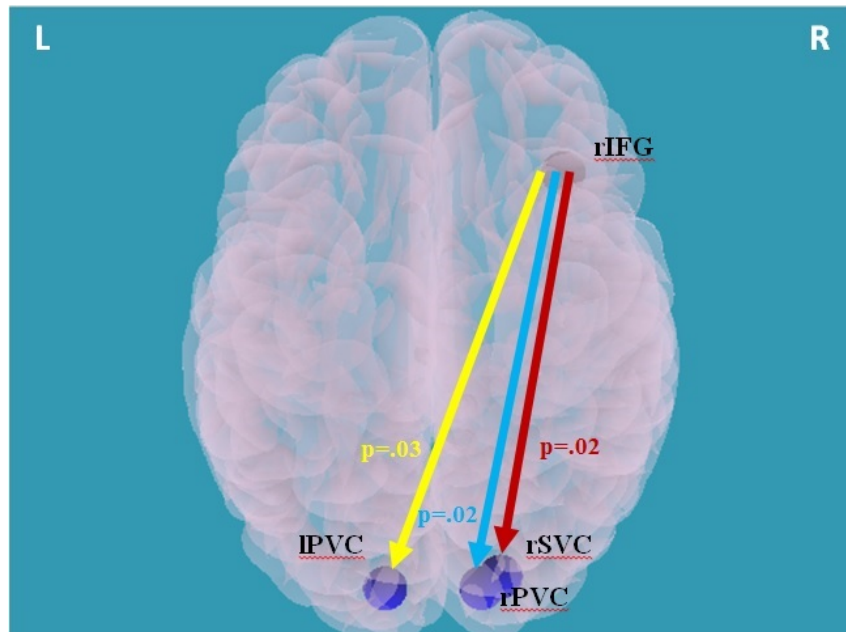


Fig. 1. ROI-to-ROI analysis with covariate inhibition: connection from rIFG to IPVC (yellow arrow), rPVC (blue arrow) and rSVC (red arrow).

045

Crossed cerebellar diaschisis in acute migraine attack under investigation as a possible mechanism for cerebellar infarctions.

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Purpose

Patients suffering from migraine with aura are considered to be at risk for cerebellar infarction, if exposed to prolonged and severe hypoperfusion during an aura. Cortical hypoperfusion, in particular, may induce crossed cerebellar diaschisis (CCD) and subsequent tissue damage. In this study, we retrospectively analyzed 112 migraine patients in order to identify potential relationships between CCD, hypoperfusion and the risk of infarction in patients with migraine with aura.

Materials and Methods

Patients with a clinically established diagnosis of migraine who underwent MR imaging including DSC-perfusion were included into the study. In patients with apparent hemispheric perfusion asymmetry, we performed a ROI-based regional perfusion analysis encompassing 18 infra- and supratentorial ROIs to account for differences of regional CBF (rCBF) and volume (rCBV). Presence of CCD was defined as >10% rCBF asymmetry (AI) in the cerebellum, and if this applied, a greater number of ROIs with AI>10% in the supratentorial contralateral hemisphere compared to the ipsilateral hemisphere.

Results

We observed perfusion asymmetries in 23/112 patients, 22 of them diagnosed as “migraine with aura (wA)”. Perfusion patterns with asymmetric rCBF and rCBV and subsequent CCD were observed in 9/23 patients (39.1%). Three further patients presented with >10% AI rCBF in the cerebellum, yet did not fulfill the criteria of CCD. CCD lateralization fully correlated with the supratentorial origin of the clinical symptoms.

Conclusions

We observed CCD in 39% of patients in “migraine (wA)”. In our series, no association with acute infarctions related to CCD was apparent, rendering it a benign phenomenon even in cases with prolonged symptom-related perfusion abnormalities exceeding 12 hrs.

O46**Risk Of Stroke Or Death Occurring On The Day Of Procedure Versus Day 1-30 After Procedure In Endarterectomy Or Stenting For Symptomatic Carotid Stenosis**

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Introduction

Stenting for symptomatic carotid stenosis (CAS) carries a higher risk of procedural stroke or death than endarterectomy (CEA). It is unclear whether this extra risk is present both on the day of procedure and within 1-30 days thereafter and whether clinical risk factors differ between these periods.

Methods

We analysed procedural risk in 4599 individual patients with symptomatic carotid stenosis who underwent CAS (n=2327) or CEA (n=2272) in four randomised trials.

Results

Compared with CEA, patients treated with CAS more often had a stroke or died on the day of procedure (110 versus 41 events, 4.7% versus 1.8%; OR 2.7, 95% CI 1.9-3.9), but not between 1 and 30 days after the procedure (56 versus 46 events, 2.4% versus 2.0%, OR 1.2, 0.8-1.7; interaction p=0.003). In patients treated with CAS, age increased and smoking history decreased the risk of stroke or death, both occurring on the day of procedure and within 30 days thereafter. In patients treated with CEA, higher level of disability at baseline was associated with stroke or death 1-30 days after the procedure. None of these risk factor associations differed significantly between time periods.

Conclusion

The increased 30-day stroke or death risk associated with CAS compared with CEA was caused by an excess in events occurring on the day of procedure. These events may potentially be prevented by operator skill and technical or medical advances. Higher age increased the risk for both immediate and delayed procedural events in CAS, mechanisms of which remain to be elucidated.

047

Diverging lesion and connectivity patterns in delayed vs. early swallowing recovery after stroke.

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Background

Knowledge about the recovery of swallowing after stroke is important to guide therapeutic decisions, including the administration of enteral tube feeding and the choice of the appropriate feeding route. We aimed to determine the localization and connectivity of lesions in early vs. delayed recovery of impaired oral intake after stroke.

Methods

Sixty-two acute ischemic hemispheric stroke patients with impaired oral intake were included in a prospective observational cohort study. Voxel-based lesion-symptom mapping and probabilistic tractography were used to determine the association of lesion location and connectivity with recovery of oral intake ≥ 7 days (indication for early tube feeding) and ≥ 4 weeks (indication for percutaneous endoscopic gastrostomy feeding) after stroke.

Results

Two distinct patterns influencing recovery of swallowing were recognized. Firstly, impaired recovery of oral intake after ≥ 7 days was significantly associated with lesions of the superior corona radiata (65% of statistical map, $p < 0.05$, figure 1). The affected fibers were connected with the thalamus, primary motor and supplemental motor areas and the basal ganglia. Secondly, impaired recovery of oral intake after ≥ 4 weeks significantly correlated with lesions of the anterior insula (54% of statistical map, $p < 0.05$, figure 2), which was connected to adjacent operculo-insular areas of deglutition.

Conclusions

Early swallowing recovery is modulated by white matter lesions disrupting thalamic and corticobulbar projection fibers. Late recovery is influenced by specific cortical lesions affecting association fibers. This knowledge will help clinicians to rapidly identify patients who are at risk of prolonged swallowing problems and might benefit from enteral tube feeding.

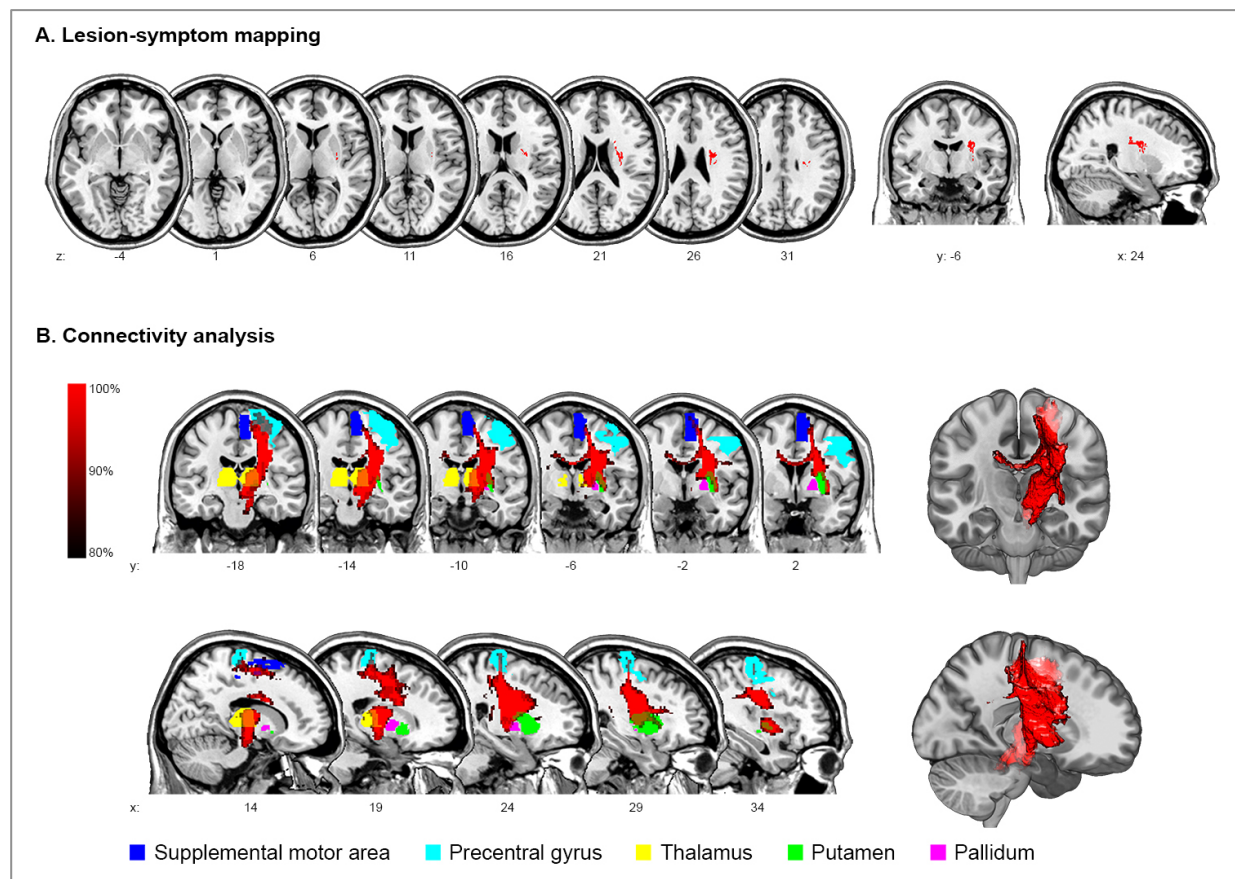


Fig 1

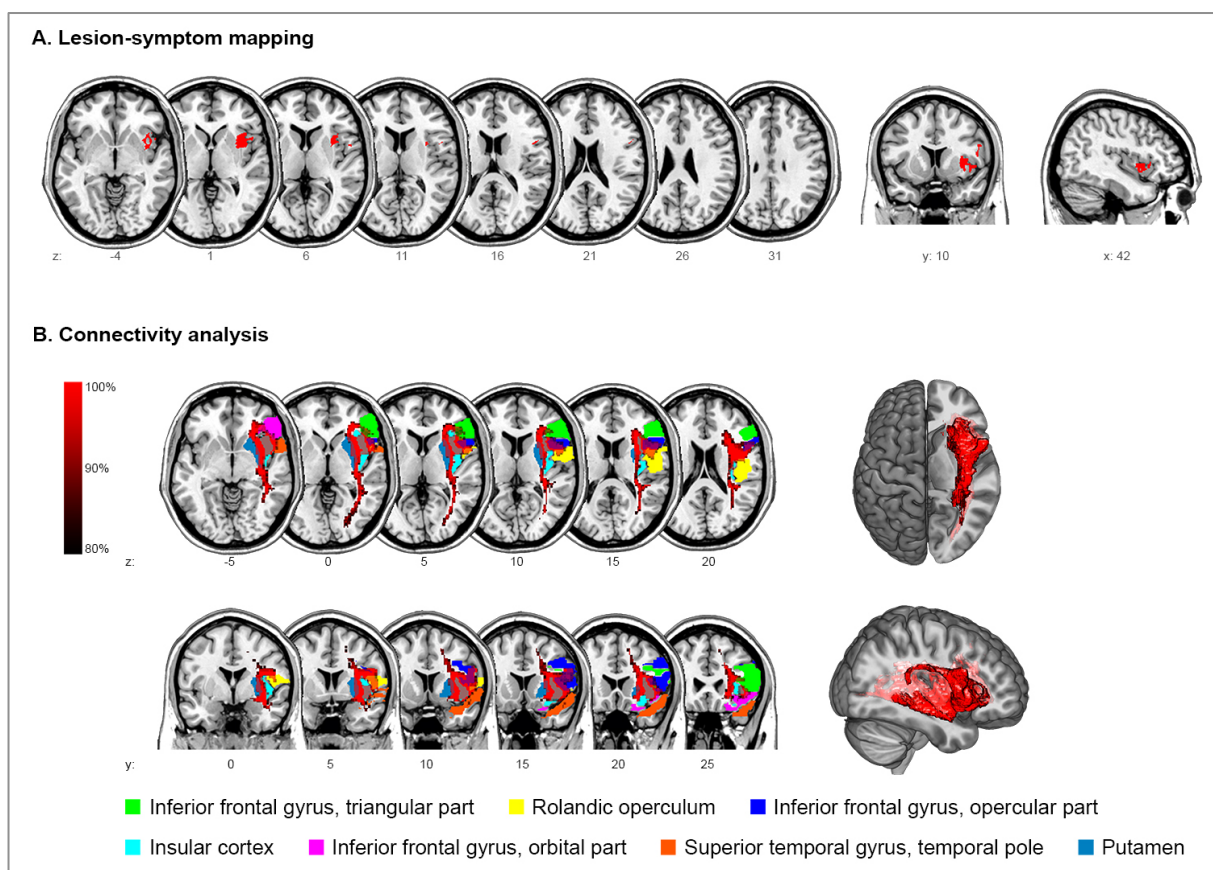


Fig. 2

048

Dose reduction in perfusion CT in stroke patients by lowering scan frequency and cine imaging length without affecting calculated infarct core and penumbra volumes

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Purpose

CT Perfusion technique (CTP) is a highly sensitive and specific imaging method for detection of ischemic brain changes. Based on calculated parameters the size of penumbra and irreversibly damaged infarct core can be judged. We wanted to evaluate whether lowering of number of scans in CTP scans affects the volume of calculated infarct core and penumbra volumes and thus if it could affect further therapeutic procedures and if potential radiation dose reduction is possible.

Methods and Materials

We have included 25 patients (9 male, 16 female, age $77,2 \pm 8,5$) who had an occlusion of M1 and/or M2 segment of MCA. The sizes of penumbra and infarct core have been evaluated using CT Neuro Perfusion application in Syngo.Via (Siemens, Germany). CTP scans were first analyzed in a standard fashion according to our in house stroke protocol. Resulting volumes measured in ml were recorded in a database. Second analysis was conducted after retrospectively increasing the time interval between sequential CTP scans and their total number (by excluding some of time points of original studies) in the same group of patients. Measurements of penumbra and infarct core volumes were repeated, recorded and compared to values obtained using our standard methods. There was no statistically significant difference between infarct core and penumbra volumes between two compared CTP protocols ($p > 0,05$).

Conclusion

Reduction of radiation exposure in CTP without objective loss of accuracy of infarct core and penumbra volume is feasible.

049

Preceding Valsalva Maneuver Significantly Associated with Pathogenic Patent Foramen Ovale (PFO) in Patients with Cryptogenic Stroke

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Background

In patients with cryptogenic stroke (CS), a patent foramen ovale (PFO) can be incidental or pathogenic. The Risk of Paradoxical Embolism (RoPE) score has been developed to determine the likelihood that a PFO is pathogenic or incidental using clinical variables. We hypothesize that echocardiographic features and conditions promoting paradoxical embolism differ between patients with pathogenic and incidental PFOs.

Methods

The International PFO Consortium collects clinical, radiological and echocardiographic data of patients with CS and PFO. In the original RoPE score, a value of 0-6 was classified as a low RoPE score and 7-10 as a high score. Since information on cortical versus deep stroke location (one of the items on the RoPE score) was not available, we used two alternative approaches to stratify for PFO pathogenicity. In a first approach, we used a 9-point score and lowered the cut-off for dichotomization by 1 point (RoPE score 0-5 vs 6-9). In a second approach, patients with a RoPE score of 6 were excluded since they could either be classified as low or high RoPE score depending on stroke location. The associations between RoPE stratum and echocardiographic features (atrial septal aneurysm (ASA), right-to-left shunt (RLS) at rest and large RLS) as well as conditions promoting paradoxical embolism (deep vein thrombosis (DVT), pulmonary embolism (PE) and Valsalva maneuver (VM) were studied.

Results

We analyzed 1044 CS patients with a PFO. Average age was 55 (SD 16) and 635 patients (61%) were male. Preceding VM was more frequent in patients with a high vs low RoPE score in both analyses: 11% vs 5% (OR: 2.1 95%CI 1.3-4.3) and 10% vs 5% (OR: 2.0 95%CI 1.2-3.6). The distribution of ASA (35% vs 34% and 32% vs 34%, in the first and the second analysis respectively), RLS at rest (28% vs 28% and 29% vs 28%), large RLS (67% vs 66% and 65% vs 66%), PE (2% vs 2% and 1% vs 2%), and DVT (4% vs 4% and 3% vs 4%) did not differ by RoPE stratum.

Conclusion

In patients with CS, preceding VM was significantly associated with pathogenic PFO, while echocardiographic features or conditions promoting paradoxical embolism were not. The formation of a significant right-to-left pressure gradient at the atrial septum level appears to play a substantial role in the pathogenicity of PFO.

O50

Early Start of NOAC After an Acute Ischemic Stroke or TIA: Risk of Intracranial Hemorrhage and Recurrent Events.

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Background

Randomized clinical trials (RCT) on non-vitamin K antagonist oral anticoagulants (NOACs) for atrial fibrillation (AF) excluded patients with acute ischemic stroke (AIS) for a minimum of 7 to 14 days after AIS. NOACs may be administered earlier than in RCT (early NOAC-start). We assessed (i) the frequency of early NOAC-starts, (ii) the rate of intracerebral hemorrhage (ICH) and (iii) recurrent AIS.

Methods

We included consecutive patients from the University Hospital Basel Stroke Center between April 2013 and September 2015 with AF hospitalized for AIS/TIA (event), and who received secondary prophylaxis with NOAC (NOACafter) or Vitamin K antagonists (VKAafter). Follow-up for ICH and recurrent events was at least 3 months. The early vs. RCT-conform NOAC-starts, and the NOACafter vs. VKAafter groups were compared.

Results

204 patients were included (mean age 79 years, 46% female, 89% AIS), for a total follow-up time of 78.25 patient-years. In the NOACafter cohort (n=155) median delay between the index event and OAC-start was 5 days (IQR 3-11), in the VKAafter cohort (n=49), 4 days (IQR 2-8). Early NOAC-starts occurred in 125 patients (81%). We observed 1 ICH ($\cong 1.3\%$ /year) and 6 recurrent events ($\cong 7.7\%$ /year), with no significant differences between the early vs. RCT-conform NOAC-start groups, nor between the NOACafter vs. VKAafter. In the NOACafter cohort, all of the 4 recurrent events occurred in the group with RCT-conform NOAC-starts.

Conclusion

Even if NOAC are often started earlier than in RCTs, the risk of ICH is low. The rate of recurrent events was six times higher than those of ICH.

051

Association of Metformin treatment with stroke severity and outcome

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Diabetes is a recognized risk factor for stroke. When stroke occurs in a patient with diabetes, clinical outcome is often less favourable. Metformin (MT) is an oral antidiabetic agent (OAD) of the biguanide class widely used as first line treatment of type 2 diabetes mellitus. MT reduces hepatic glucose production and intestinal glucose resorption, and increases glucose uptake in muscle tissue. In addition to its glucose-lowering effects, beneficial cardiovascular outcomes and lower mortality rates have been reported for patients taking MT possibly through modification of 5' AMP-activated protein kinase (AMPK) activity. Our goal was to study the effect of MT pre-treatment on stroke severity and outcome, including success of thrombolytic therapies.

In this retrospective analysis (2014-2016), patients with previously known or newly diagnosed diabetes presenting with acute ischemic stroke were selected from the Swiss Stroke Registry (SSR). Data was analyzed with respect to epidemiological characteristics, risk factors, pre-stroke disability (mRS), symptom severity (NIHSS) and outcome after 3 months (mRS). The type of antidiabetic treatment was then assessed. Statistical analysis was performed using nonparametric tests for continuous and chi-square test for nominal parameters.

We identified 100 patients with ischemic stroke and diabetes. Of these, 48 patients received MT, while 52 received other or no treatment (29: no treatment, 19: dipeptidylpeptidase-3 inhibitors, 17: sulfonamide, 24: insulin or a combination of treatments). Patients receiving metformin (MT+) had a significantly lower pre-stroke mRS compared to those without metformin (MT-): median (IQR) 0 (1) versus 1 (2) $p = 0.037$. There was a higher frequency of smokers and additional antihypertensive medication in the MT+ group. The distribution of other risk factors, admission glucose, frequency of thrombolytic treatments, stroke etiology and 3month mRS was similar between both groups, with a tendency for a lower admission NIHSS in the MT+ group: median (IQR) 4 (5) vs. 7 (8) $p = 0.092$.

In conclusion, patients with diabetes and ischemic stroke pretreated with MT had less pre-stroke disability than patients without MT treatment. We conducted a sample size calculation estimating that we would need to include 138 patients for a statistically sound analysis. We are currently collecting more patient data and planning a multicenter SSR analysis to assess the effect on thrombolysis success.

P01

Targeting deregulated AMPK and mTORC1 pathways in DM1 improves muscle function via splicing-dependent and -independent mechanisms

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Myotonic Dystrophy type I (DM1) is a disabling multisystemic disease affecting skeletal muscle. The disease is caused by expanded (CTG)_n repeats in the DMPK gene. RNA-hairpins formed by the elongated transcripts lead to sequestration of splicing factors, and thereby to mis-splicing of different genes. Although strategies have been tested to limit splicing defects, no causal treatment is available for the disease. Muscle atrophy in DM1 has been related to perturbation in catabolic processes, even though extensive investigations are lacking. Here, we investigated whether DM1-associated muscle alterations may be related to a deregulation of central metabolic signalling and/or of the autophagy process. We showed that muscles from HSALR mice, a well-characterized mouse model for DM1, maintain active mTORC1 signalling under starved conditions, while Akt is efficiently inhibited. Additionally, AMPK was not fully activated in muscle from starved mutant mice, which might be related to splicing-dependent CaMKII deficiency. Moreover, we observed that autophagy flux is impaired in HSALR muscle and in human DM1 myotubes, which may arise from the deregulation of AMPK/mTORC1 signalling. Most importantly, normalization of these pathways with pharmacological or dietary approaches potentially improved skeletal muscle strength and significantly reduced myotonia in HSALR mice. In particular, the AMPK agonist, AICAR, but not metformin, a drug known to induce the pathway, led to a striking amelioration of the relaxation time of mutant muscle, together with partial splicing correction. On the other hand, rapamycin, a mTORC1 inhibitor, and prolonged low-protein diet both reduced myotonia but not DM1-related mis-splicing, suggesting that alternative, splicing-independent mechanisms could improve muscle function in DM1. These findings highlight the involvement of AMPK/mTORC1 imbalance in DM1 muscle pathophysiology, and open new avenues regarding therapeutic options for the disease.

P02**Severe Impact of bladder Overactivity on Lower limb's Spasticity in a Case of Acute Spinal Cord Injury**

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Based on a special case we will demonstrate the impact of neurogenic detrusor overactivity on the shaping of lower limb's spasticity in an acute spinal cord injured young man level D3 ASIA A due to traumatic cause. We know that a spastic syndrome of the lower limbs can be triggered by bladder overactivity and vice versa.

Most cases of traumatic spinal cord injury (SCI) with spastic paraplegia develop limb and trunc spasticity below the neurologic level within the first to sixth month¹. To reach the peakedness may need up to 18 month.

In this young man the spastic paraplegia envolved in time from the third month but increased unusual exponentially. Despite all conservative therapy, it was not possible to calm it down. The spastic's severity (Ashworth IV) made it nearly impossible to follow a correct rehabilitation. For that reason we early implanted an intrathecal baclofen pump just in the fourth month after accident.

In the following weeks we rised the dosage rapidly up to i.t. 232.1µg/d in 11th month after accident.

Parallel to that his bladder became the same way rapidly spastic. He had strong desire to void, could not control the voiding, was urinary incontinent and had high residual volume and urinary tract infections. He was strongly bothered. The urodynamic finding shows high intravesical pressure duo to detrusor overactivity and detrusor-sphincter-dyssynergia (DSD). All conservative and minimally interventional therapy was not successful enough. We decided similar to our paraplegia colleagues to do surgery very early in his SVI career at 13th month after accident. Intraoperatively we found a strongly thickened bladder wall as a sign for overactivity. Immediately after surgery just on the ward the patient loosed his lower limb spasticity. There was no elevated muscle tonus any more. So we could lower the baclofen dosage over next month's up to minimal flowrate of 3.4µg/d in the 16th month. In May 2016 (20th month) we explanted the pump.

There was an additional interference of the intrathecal baclofen therapy: the tonus of the external urethral sphincter was initially very low after surgery, so he has urinary incontinence. Only after lowering the baclofen dosage and slightly rising spasticity in the lower limbs he develops again a DSD that made him continent with a good bladder capacity.

We can show a correlation between Ashworth scale, baclofen dosage and bladder pressure in this case.

Conclusion

If there is an early high spasticity level in acute phase of SCI we have to think also about bladder overactivity that may trigger these limb spasticity additionally.

Any indication for a surgical treatment within the first year has to be proven very carefully.

This case demonstrates that a sometimes an early pump implantation may be helpful just to make a rehabilitation even possible. In times of uncontrolled spasticity and bladder dysfunction this patient was not able to train transfer, to make sport, to go with the wheelchair and so on. So his rehabilitation time was prolonged.

Reference

Hiersemenzel et al. 2000 Dissertation 2006 ETH Dr Roland Müller: Lokomotions- und Reflexaktivität bei kompletter Querschnittlähmung: Einflussfaktoren und Zeitliche Entwicklung

P03**The effect of vibrotactile biofeedback of trunk sway on balance control in multiple sclerosis**

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Background

Patients with multiple sclerosis (MS) suffer from diminished balance control due to slowed sensory conduction and possibly delayed central processing. Vibrotactile biofeedback of trunk sway has been shown to improve balance control in patients with peripheral and central vestibular disorders.

Objective

To measure the effects of vibrotactile feedback training on trunk sway in MS during different stance and gait tasks.

Methods

In total, 10 MS patients (6 relapsing-remitting, 2 secondary-progressive and 2 primary-progressive MS, mean age 46.8 ± 7.7 years, 40% male, median EDSS 4.0 [range 2.5 - 6.0]) with complaints of balance impairment participated in a randomized controlled crossover study in which 7 different stance and gait tasks were trained with and without sway angular feedback for stance and sway angular velocity feedback for gait tasks. Dizziness Handicap Inventory (DHI) questionnaires were used to measure the subjective balance deficits. An assessment sequence of 12 stance and gait tasks was performed once before and twice after the training sequence including standing on one or two legs with eyes open and closed on a firm or foam surface, tandem stance eyes open and closed, walking 8 tandem steps eyes open and closed, walking over barriers, walking 8 m eyes open and 3 m eyes closed. Trunk sway was measured with body-worn gyroscopes mounted near the body's centre of mass, in the centre of the lower back at vertebral level L3-L5. Head mounted vibrotactile biofeedback of lower trunk sway was provided during one crossover training arm and the following second but not the third assessment sequence.

Results

In most tasks, biofeedback led to a marginal decrease in sway and increase in sway angular velocities for stance tasks and vice versa for gait tasks when compared to training without biofeedback. For example, walking eyes open resulted in a decreased sway angular velocity. The greatest changes during gait were found in the pitch direction of trunk sway (-13.87 ± 6.03 degree/sec, $p=0.02$). Effects diminished after biofeedback was removed.

Conclusions

One session of vibrotactile biofeedback of trunk sway beneficially effects stance and gait balance control of MS patients compared to training without biofeedback. Planned trials with more intensive vibrotactile feedback training (2 times per week for 2 weeks) are expected to yield greater effects.

P04**A new generation in Aphasia therapy – Tablet-based rehabilitation of speech and language**

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Aphasia is the loss or impairment of language functions that occurs following brain damage due to stroke, trauma, tumors or infection. This disorder hinders the ability to understand and be understood and can be affected in different combinations and levels of severity. Stroke affects about 15,000 patients per year in Switzerland and nearly 30% of the stroke cases develop aphasia. Affected patients undergo intensive face-to-face speech and language (SLT) therapy aiming to improve their communication and language skills. Although SLT has been proven to substantially alleviate symptoms, their success depends mainly on the frequency of the therapy, duration of therapy and partly on patient compliance, resource availability, finances and travel hurdles. However, it is challenging for both therapists and patients to cope with the demanding need of therapy time. Individualized computer-mediated, tablet-based aphasia tele-rehabilitation are more intuitive to use and can complement conventional SLT. Moreover, since aphasia is highly individual, the level of difficulty and the content of tasks have to be adapted continuously by the speech therapists. Computer-based assignments allow patients to train independently at home and thus increasing the frequency of therapy. Aim: The aim of this project was to develop a tablet application that enables patients to train language related tasks autonomously and, on the other hand, allows speech therapists to assign exercises to the patients and to track their results online. Methods: A user management system separates the application into two parts (patient interface, therapist interface). The patient interface is implemented using Objective-C and contains 520 exercises which were developed in close-collaboration with speech therapists. New exercises can be created by therapists using a web interface. Usability and acceptance of both interfaces was tested in 15 healthy participants, 5 aphasia patients, and 5 speech therapists. System Usability Scale (SUS) was used as main outcome measure. Results: SUS scores for the patient interface are 98/100 for patients, 92.7/100 for healthy, and 68/100 for the therapist interface. Conclusions: The novel therapy application was well accepted by patients and therapists. Usability of the therapist interface is currently being tested. With tablet based applications, both patients and therapists can benefit from an intuitive, touch-based reliable product which fits well with the current trend

P05**Simultaneous EEG and Arterial Spin Labeling (ASL): safety tests and preliminary results**

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Background

Arterial spin labeling (ASL) is a noninvasive technique that uses arterial blood as an endogenous tracer to quantify cerebral blood flow (CBF). In respect to the qualitative assessment of EEG-fMRI, ASL-EEG combination estimate pathological blood changes related to interictal epileptic activity. Our aim was to demonstrate the feasibility of EEG-ASL with regard to safety and signal quality.

Methods

High-density EEG was acquired simultaneously with pseudo-continuous ASL in one phantom and two healthy subjects. Temperature at the level of EEG electrodes was monitored with 4 MR-compatible sensors. In the subjects, two 7 minutes functional fMRI runs were acquired with eyes open/closed blocks and rhythmic hand finger clenching. Gradient and pulse artefacts in EEG were corrected with the methods used conventionally for EEG-fMRI. For eyes open/closed paradigm the alpha component extracted from EEG was used as regressor in a GLM model. For the motor paradigm we used the block design timing.

Results

Temperature increase did not exceed 0.5°C. MR-related artifacts were successfully corrected. EEG ICA decomposition was able to capture the alpha rhythm in one single component. Alpha power modulation induced a decrease of CBF in occipital regions whereas motor tasks produced an increase in primary motor cortex.

Conclusion

Simultaneous EEG-ASL can be recorded safely. These preliminary results are promising for the acquisition of quantitative functional activity of the brain. Additional tests are required to demonstrate the feasibility in event-related design to prove its ability to detect CBF changes associated with interictal epileptic events.

P06**Repeated Intravenous Thrombolysis In Patients With Early Recurrent Ischemic Stroke**

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Objective

Intravenous thrombolysis (IVT) given within 4.5 hours from symptom onset is effective and safe in patients with acute ischemic stroke. Its use in patients with prior infarct within the preceding 3 months is contraindicated due to an assumed higher risk of intracerebral hemorrhage (ICH). In addition, apart from the beneficial thrombolytic effects, tissue plasminogen activator itself is capable of aggravating ischemic damage by promoting neurotoxicity and blood-brain barrier disruption. However, as patients with early (<3 months) recurrent stroke (ERS) have largely been excluded from thrombolysis randomized controlled trials (RCT), effectiveness and safety of repeated IVT is essentially unknown in these patients. We here report the largest case-series of repeated IVT in ERS.

Methods

We retrospectively searched the databases of eight European stroke centers for patients with ERS, who received IVT for both strokes. Demographics, clinical and radiological data, bleeding complications and functional outcome were analyzed.

Results

We identified 19 ERS patients receiving repeated IVT. Mean age was 68 ± 12 years and 37% were female. Mean inter-thrombolysis interval was 33 days (range: 2-82). Functional independence ($mRS \leq 2$) was achieved in 79% of patients after the first and in 47% after the repeated IVT, respectively. There was no symptomatic ICH.

Conclusion

Our data challenges the current acute treatment paradigms and strongly encourages reconsideration of the IVT exclusion criterion "prior stroke within 3 months". As RCTs for these rare cases are not likely, larger registries might serve to identify selection criteria for the safe use of repeated IVT in ERS.

P07**MiRNA 150-5p Adds Prognostic Information After Acute Ischemic Stroke**

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Background

MicroRNAs (miRNAs) are involved in post-transcriptional gene regulation influencing disease progression and prognosis. MiR-150-5p regulates proinflammatory cytokines, mediators of cellular communication in the ischemic brain, as well as vessel integrity. We aimed at evaluating the incremental prognostic value of miR-150-5p after ischemic stroke.

Methods

In a prospectively enrolled ischemic stroke cohort, levels of miR-150-5p were measured within 72 hours of symptom onset in 329 patients. The primary endpoint was functional outcome (modified Rankin Scale score <3 or 3–6), the secondary endpoint was mortality within 90 days. Logistic regression and cox proportional hazards models were fitted to estimate odds ratios (OR), respectively hazard ratios (HR) and 95% confidence intervals (CI) for the association between miR-150-5p and the primary and secondary endpoints. The discriminatory accuracy was assessed with the area under the receiver-operating-characteristic curve (AUC) and the incremental prognostic value was estimated with the net reclassification index (NRI).

Results

After adjusting for demographic and vascular risk factors, lower miR-150-5p levels were independently associated with mortality (HR 0.21 [95% CI, 0.08–0.51], $p=0.001$) but not functional outcome (OR 1.10 [95% CI, 0.54–2.25], $p = 0.79$). Adding miR-150-5p to the multivariate model improved the AUC from 0.91 (95% CI, 0.88–0.95) to 0.92 (95% CI, 0.88–0.96), LRT- p -value<0.001, and resulted in a NRI of 37.3% (95% CI, 0.28–0.52).

Conclusion

In patients with ischemic stroke, miR-150-5p is a novel prognostic biomarker, improving risk classification beyond traditional risk factors.

P08**Understanding Recovery from Stroke through Lesion Load on Structural Brain Areas**

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A stroke is generally followed by clinical treatment in the acute phase, and a subsequent time-consuming rehabilitation step in the chronic phase of the disease. To optimize the rehabilitation treatment in terms of minimizing the patient's functional and/or cognitive impairment, as well as its cost effectiveness, it is essential to understand the processes in the brain that govern recovery. This work investigates the level of impairment and outcome prognosis by computing the lesion overlap with distinguished structural brain areas.

For the overlap with the structural brain areas, a DTI-based brain atlas from the Johns Hopkins University (Oishi et al., NeuroImage, 2009) is employed. This atlas consists of 176 cortical and subcortical brain regions. The analysis is conducted with respect to the NIHSS score recorded three month after the incidence. The relationship between brain regions and the recorded NIHSS is examined by means of correlation tests.

The study population consists of 74 patients, with heterogeneous lesion sites and functional/cognitive impairments. First, it is investigated whether the lesion load on structural areas is predictive of the NIHSS. Second, for these structural areas it is investigated whether cortical or subcortical regions are more meaningful for the impairment. This latter analysis is interesting in comparison with the literature as most studies conducted so far are mainly concerned with the corticospinal tract. The correlation analysis between structural lesion load and outcome, measured by the NIHSS, indicates that the white matter structures are indeed of great importance. This seems to be true for all levels of impairment. However, the analysis also reveals that the cortical regions should not be neglected, as some of them correlate significantly with the NIHSS. Also, there is an indication that the level of impairment is mainly determined by the amount of lesion load on a group of important regions, rather than by mutually independently affected brain regions.

In a future work we will compute the lesion load additionally on functional brain networks. With this, we will be able to understand more deeply which regions and networks are mainly involved in recovery from stroke. Furthermore, we will use machine learning techniques to make a prognosis for the clinical measure after three months based on the lesion loads predicted from imaging during the acute phase of the disease.

P09**Stratification of Patent Foramen Ovale (PFO) Pathogenicity Using the RoPE Score Differs in Women**

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Background

A patent foramen ovale (PFO) discovered in patients with cryptogenic stroke (CS) may be incidental or pathogenic. Recently, a Risk of Paradoxical Embolism (RoPE) score has been proposed to stratify patients by their PFO pathogenicity. Based on this score, the probability that a PFO is incidental (rather than pathogenic) increases with advancing age, deep stroke location, or the presence of cardiovascular risk factors (RF). Given that RF accumulate at a later age in women than in men, we hypothesize that there are gender differences in the variables used for RoPE score calculation.

Methods

The distribution of RF (history of hypertension, diabetes or stroke/TIA, current smoking, and age categories as defined in the original RoPE score publication) was compared by sex in the entire cohort of 1044 CS patients as well as within the groups with low (0-5) and high (7-10) RoPE scores (due to lacking information on cortical versus deep stroke location, we excluded all patients with a RoPE score of 6, since they could be either classified with low or high RoPE score depending on stroke location). Furthermore, for each patient we calculated the age impact ratio (AIR): the points assigned for the corresponding age category divided by the RoPE score. Gender comparisons of AIR were drawn in the entire cohort and within the RoPE score strata.

Results

Average age was 55.5 years and 635 patients (61%) were male. In the entire cohort, the distribution of age categories and RF as well as AIR did not differ between men and women. In the higher RoPE stratum (PFO likely pathogenic), women were younger than men (median, 38 years vs 45 years, $P=0.036$). The distribution of RF and the AIR did not differ between sexes. In the lower PFO stratum (PFO likely incidental), men were younger than women (median, 62 years vs 66 years, $P=0.011$). The AIR was lower in women than in men (mean, 0.24 vs 0.29, $P=0.013$). There were no gender differences in the distribution of RF.

Conclusions

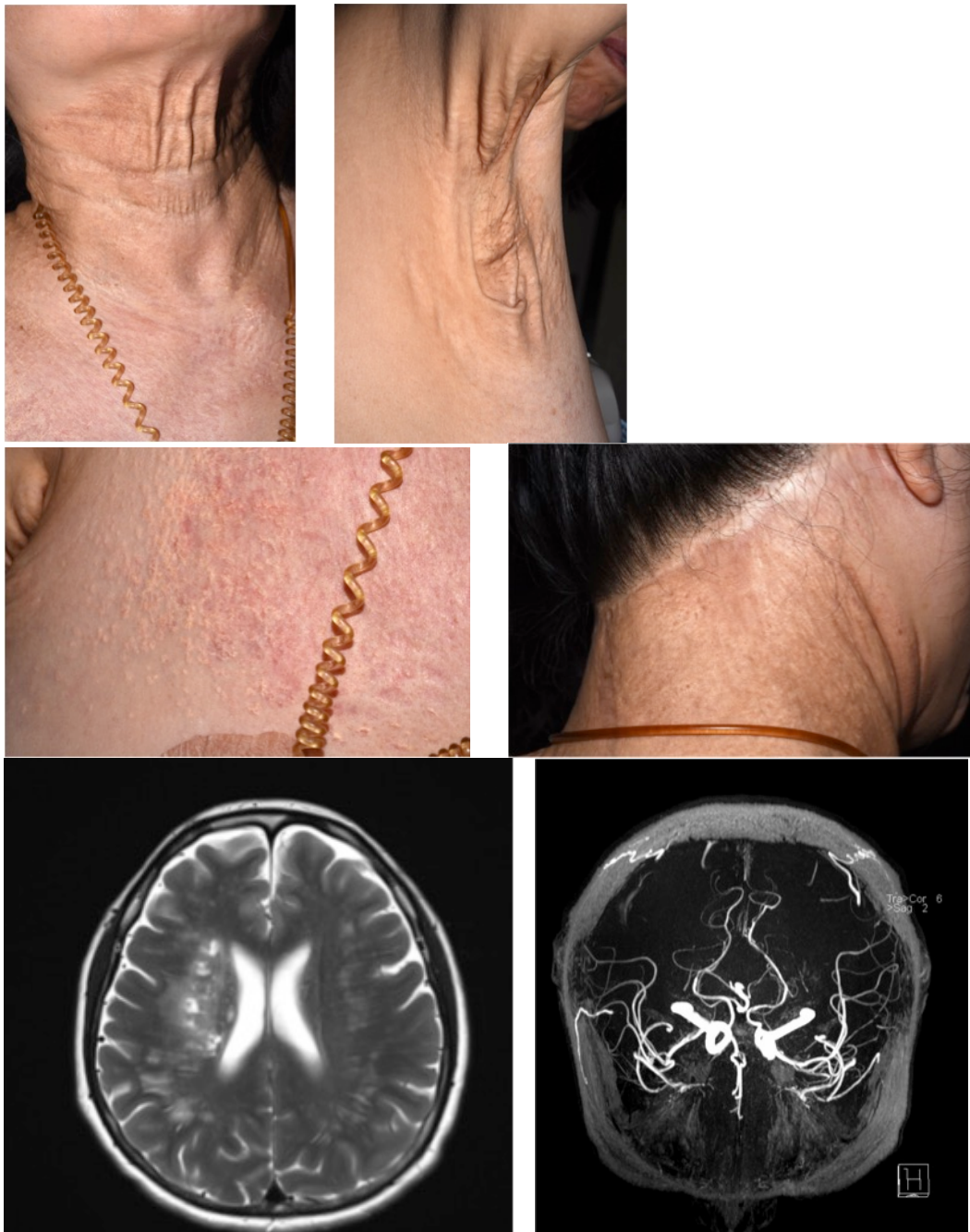
There are significant gender differences in age among patients with CS and PFO, with women being younger than men in the higher RoPE stratum and vice versa in the lower RoPE stratum. More women than men are classified as having an incidental PFO because of their advancing age rather than the accumulation of RF.

P10**Pseudoxanthoma elasticum and stroke : a dermatological condition associated with cerebral vessel disease**

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Stroke of determined origin other than cardioembolism, atherosclerosis and small vessel disease accounts for approximately 30% of stroke in young patients. We describe the case of a 52 year old woman only known for mild hypertension who presented with right middle cerebral artery ischemic stroke, associated with multiple artery stenosis of unknown etiology. The skin examination showed several lesions (mainly confluent yellow flat papulae on the neck and axilla) consistent with Pseudoxanthoma Elasticum (PXE), which was proven on genetic testing. This inherited genetic disorder due to a mutation in the ABCC6 gene affects elastic fibers of the skin and small vessel walls, increasing risk of atherosclerosis and hypertension. We highlight the importance to recognise it as a potential cause of stroke in young patients, especially when facing the typical skin lesions.



P11**Quantitative assessment of somatosensory abnormalities in patients with central post-stroke pain of thalamic origin**

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Background

Central post stroke pain (CPSP) is a severe neuropathic pain syndrome that develops days to months (sometimes even years) after a vascular lesion in the central nervous system, often in the thalamus. If CPSP patients could be characterized by a specific somatosensory phenotype, this may allow the early identification of stroke patients at risk of developing CPSP. Moreover, a better understanding of this phenotype may shed light on the underlying pathophysiological mechanisms.

Objectives

To systematically examine somatosensory deficits in patients with CPSP of thalamic origin.

Methods

We examined 11 patients with thalamic CPSP (6 men, mean age 60.8 years). Standardized quantitative sensory testing (QST) was performed at both hands. We compared the side affected by pain with the unaffected arm for various sensory submodalities. A paired T-test was used for normally distributed and Wilcoxon test for non-normally distributed variables. We also compared the results with normative values from healthy volunteers.

Results

Median spontaneous pain intensity was 5/10 on a visual analogue scale. The average threshold for light touch (mechanical detection threshold, MDT) was significantly higher on the affected vs. the unaffected hand (mean $\pm$ SD: 11.1 $\pm$ 7.9 vs. 3.86 $\pm$ 3.2 mN; $p=0.008$). The vibration detection threshold was on average lower on the affected vs. unaffected side [median (range): 7.2 (0-8) vs. 8 (7-8); $p=0.012$]. We found no significant differences in temperature and pain perception thresholds. Compared to normative values, the MDT on the affected side was abnormally high in most patients (7/11), while the vibration sense was reduced in 3 patients. Regarding positive symptoms, we detected unilateral dynamic mechanical allodynia on the affected side in 4/11 patients and unilateral cold allodynia in 2 patients (both with normal cold detection thresholds).

Conclusions

Reduced sensation to light touch and vibration were the most frequent somatosensory deficits on the affected side of our patients. This finding does not support the view that a specific dysfunction of the lateral spinothalamic tract is involved in the pathogenesis of thalamic CPSP. Cold allodynia was not accompanied by cold hypesthesia, suggesting that hypersensitivity does not necessarily require deafferentation.

P12**Action Tremor of The Hands as Main Manifestation of Tick-Borne Encephalitis**

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Introduction

Tick-borne encephalitis (TBE) presents with a variable clinical picture. A quarter of people with seroconversion develop severe neurologic disease. After an incubation period of one week, a first viraemic phase with fever, fatigue, malaise or headache may be observed. In a second phase, a variable clinical picture, ranging from oligosymptomatic mild meningitis to severe encephalitis, myeloradiculitis and possibly death, can be seen. TBE virus is transmitted by *Ixodes* spp. ticks and is present in endemic areas which cover large parts of Switzerland. The number of reported TBE cases tends to rise and reached around 100 - 200 cases in Switzerland per year. No specific therapy is available.

Case

A 72-year-old otherwise healthy man presented with a one-week history of fatigue and a 2-day history of chills, fever and headache. Especially, he reported a new tremor of the hands. He was barely able to write. No recovery was observed after initiation of antibiotic treatment with cefuroxime, which was started by his family doctor. The patient remembered a tick-bite a few months before admission. The physical examination revealed a temperature of 38.2°C, but no rash and no meningism. Neurologically, the patient showed a postural and intention tremor of the arms and also a slight intention tremor of the legs. CT and MRI of the head showed no abnormalities. Lab work-up showed thrombocytopenia, but no signs of inflammation. Cerebrospinal fluid analysis revealed slightly elevated leukocyte counts and slightly elevated protein. Serum serology was positive for TBEV IgM and IgG. The patient received intense neurorehabilitating training in a specialized clinic and could be released without sequelae.

Conclusion

TBE can be a Chameleon. We report an unusual presentation with predominantly an action tremor of the arms that imitated a neurological movement disorder like an essential tremor syndrome. The cause may have been an encephalitic involvement of cerebellar structures. TBE is an important differential diagnosis in patients presenting with otherwise unexplained neurologic symptoms usually together with fever in endemic areas. It can easily be diagnosed by serological testing of the serum, also in the setting of a general practitioner, and prevented by vaccination.

P13**Effect of Ocrelizumab on MRI Inflammatory and Neurodegenerative Markers of Disease in Patients With Relapsing Multiple Sclerosis: Analysis of the Phase III, Double-blind, Double-dummy, Interferon Beta-1a- controlled OPERA I and OPERA II Studies**

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Objective

To evaluate the effect of ocrelizumab vs interferon beta-1a (IFN β -1a) on MRI outcomes in patients with relapsing multiple sclerosis enrolled in two identical Phase III, randomized, double-blind, double-dummy trials (OPERA I and OPERA II).

Background

In MS, there is an interdependence between inflammation and neurodegeneration, which could be mediated through B cell and T cell interactions. MRI is used to evaluate inflammatory and neurodegenerative markers of MS. Ocrelizumab is a humanized monoclonal antibody that selectively targets CD20+ B cells.

Methods

In OPERA I and OPERA II, patients were randomized (1:1) to receive ocrelizumab 600mg via intravenous infusion every 24 weeks or subcutaneous IFN β -1a44 μ g three times weekly over 96 weeks. Brain MRI endpoints included the total number of T1 gadolinium-enhancing lesions, new/enlarging T2 hyperintense lesions, and new T1 hypointense lesions at weeks 24, 48, and 96, and change in whole brain volume from baseline and week 24 to week 96.

Results

Compared with IFN β -1a, ocrelizumab reduced T1 gadolinium-enhancing lesions by 94% in OPERA I and 95% in OPERA II (both $p < 0.0001$); new/enlarging T2 hyperintense lesions by 77% in OPERA I and 83% in OPERA II (both $p < 0.0001$); new T1 hypointense lesions by 57% in OPERA I and 64% in OPERA II (both $p < 0.0001$); and brain volume loss from baseline to week 96 by 23.5% ($p < 0.0001$) and 23.8% ($p = 0.0001$) and from week 24 to week 96 by 22.7% ($p = 0.0042$) and 14.9% ($p = 0.0900$) in OPERA I and OPERA II, respectively.

Conclusions

Ocrelizumab significantly and consistently suppressed inflammatory and neurodegenerative markers of disease on MRI vs IFN β -1a in OPERA I and OPERA II over 96 weeks, with near-complete elimination of new T1 gadolinium-enhancing lesions following the first dose. The majority of new/enlarging T2 lesions and new T1 hypointense lesions occurred before week 24 and significantly declined thereafter.

Supported by F. Hoffmann-La Roche Ltd.

P14**Efficacy of Ocrelizumab in Patients With Relapsing Multiple Sclerosis: Pooled Analysis of Two Identical Phase III, Double-blind, Double-dummy, Interferon Beta-1a-controlled Studies**

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Objective

To evaluate the efficacy of ocrelizumab compared with interferon beta-1a (IFN β -1a) through pooled analysis of efficacy endpoints in OPERA I and OPERA II.

Background

MS pathogenesis is understood to involve two distinct but overlapping mechanisms, with early inflammation and concurrent or subsequent neurodegeneration. Ocrelizumab, a humanized monoclonal antibody that selectively targets CD20+ B cells, was superior in reducing annualized relapse rate (ARR) versus IFN β -1a in OPERA I and OPERA II, two identical Phase III, randomized, double-blind, double-dummy trials in relapsing MS.

Methods

Pooled analyses of the OPERA I and OPERA II efficacy endpoints were considered to be valid if the treatment difference between the ocrelizumab- and the IFN β -1a-group for ARR through week 96 and ≥ 12 -week confirmed disability progression (CDP) was broadly consistent between the two studies; i.e. $p > 0.1$ for study-by-treatment group interaction or $p \leq 0.1$ for study-by-treatment group interaction and both within-study treatment differences are in the same direction. Pre-specified pooled analyses included ≥ 12 -week and ≥ 24 -week CDP and ≥ 12 -week confirmed disability improvement (CDI) through week 96.

Results

Consistency of baseline characteristics and treatment effects across both studies met pre-determined criteria for pooled efficacy analysis. Compared with IFN β -1a, ocrelizumab showed a 47% reduction in adjusted ARR ($p < 0.0001$) and reduced the risk of 12-week CDP by 40% ($p = 0.0006$) and 24-week CDP by 40% ($p = 0.0025$). For pooled data, the proportion of ocrelizumab-treated patients that achieved CDI at 12 and 24 weeks was 20.7% and 15.6% versus 15.6% and 11.6%, respectively, for IFN β -1a-treated patients, representing a 33% and 36% relative improvement (relative risk 1.33 [$p = 0.0194$] and 1.36 [$p = 0.0343$]), respectively. Ocrelizumab showed an 18.8% reduction in brain atrophy vs IFN β -1a ($p = 0.0015$).

Conclusions

Pooled analyses of OPERA I and OPERA II efficacy endpoints showed that ocrelizumab significantly suppressed disease worsening and enhanced disability improvement over the 96-week period compared with IFN β -1a.

Supported by F. Hoffmann-La Roche Ltd.

P15**The SeLECT score: a novel tool to predict seizures after ischemic stroke.**

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Background

Stroke is the most common cause of acquired epilepsy in adults. The process underlying development of epilepsy, called epileptogenesis, typically takes weeks to years. This latent period offers time for diagnostic and therapeutic procedures to prevent epileptogenesis. An instrument to predict those who will develop seizures and would benefit from these procedures is not available. We developed and externally validated a prognostic model of late seizures after ischemic stroke.

Methods

Using backward elimination of a multivariate logistic regression model, we derived a score (SeLECT) in 1200 ischemic stroke patients from the Stroke and Epilepsy Registry of Eastern Switzerland (SERES) to predict late seizures (> 7 days after insult) as primary outcome measure. The secondary outcome were recurrent late seizures. We externally validated this score in 1427 patients from three independent international cohorts (Austria, Germany, Italy) and assessed its performance with the concordance (c) statistic, calibration plots, and the Hosmer-Lemeshow calibration test.

Results

Overall, 138 of 2627 (5%) patients suffered late seizures and they were recurrent in 90 (3%). The lowest SeLECT value (0 points) was associated with a 5-fold decrease of late seizure risk, whereas the highest value (10 points) predicted a 12-fold increase of relative risk (10-fold decrease vs. 10-fold increase for recurrent seizures). The model had an overall c statistic of 0.76 in validation cohorts. Calibration plots and nonsignificant Hosmer-Lemeshow tests ($p > 0.3$) indicated good fit of predicted and observed outcomes.

Conclusions

This easily applicable instrument was a good predictor of late seizures after stroke in triple external validation. The SeLECT score has the potential to individualise clinical care by identifying those who would benefit from optimal management and appropriate follow-up. It can inform the selection of an enriched population for antiepileptogenic treatment trials and guide the recruitment for biomarker studies of epileptogenesis.

P16**A retrospective analysis of efficacy in McDonald 2010 multiple sclerosis (MS) patients in the ORACLE-MS study**

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Background

In the ORACLE-MS study, patients with clinically isolated syndrome (CIS) at high risk for MS were randomised to cladribine tablets 3.5 or 5.25 mg/kg bodyweight (cumulative over 2 years) given annually in short-duration courses. Risk of clinically definite MS (CDMS) conversion was significantly reduced by cladribine vs. placebo.

Methods

This retrospective analysis assessed the effects of cladribine on time to next relapse/disability progression in ORACLE-MS patients who met the McDonald 2010 MS criteria at baseline, as well as in patients not fulfilling these criteria (i.e., “true” CIS).

Results

At baseline, 36.2% of patients (223/616) met the McDonald 2010 diagnostic criteria. In this subgroup (Figure 1), cladribine 3.5 mg/kg (n=68) significantly reduced the risk of next relapse/disability worsening versus placebo (n=72, HR 0.26, 95%CI 0.12–0.58; p=0.0009), consistent with a 74% risk reduction. In “true” CIS patients (Figure 2), cladribine 3.5 mg/kg (n=138) significantly reduced the risk of next relapse/disability worsening (i.e. CDMS) versus placebo (n=134, HR 0.37, 95%CI 0.22–0.63; p=0.0003), consistent with a 63% risk reduction. In each subgroup, the risk of next relapse/disability worsening was also reduced with cladribine 5.25 mg/kg.

Conclusions

Compared with placebo, cladribine 3.5 mg/kg significantly reduced the risk of relapse/disability worsening in patients meeting both up to date definitions for MS or CIS.

Study supported by Merck KGaA, Darmstadt, Germany

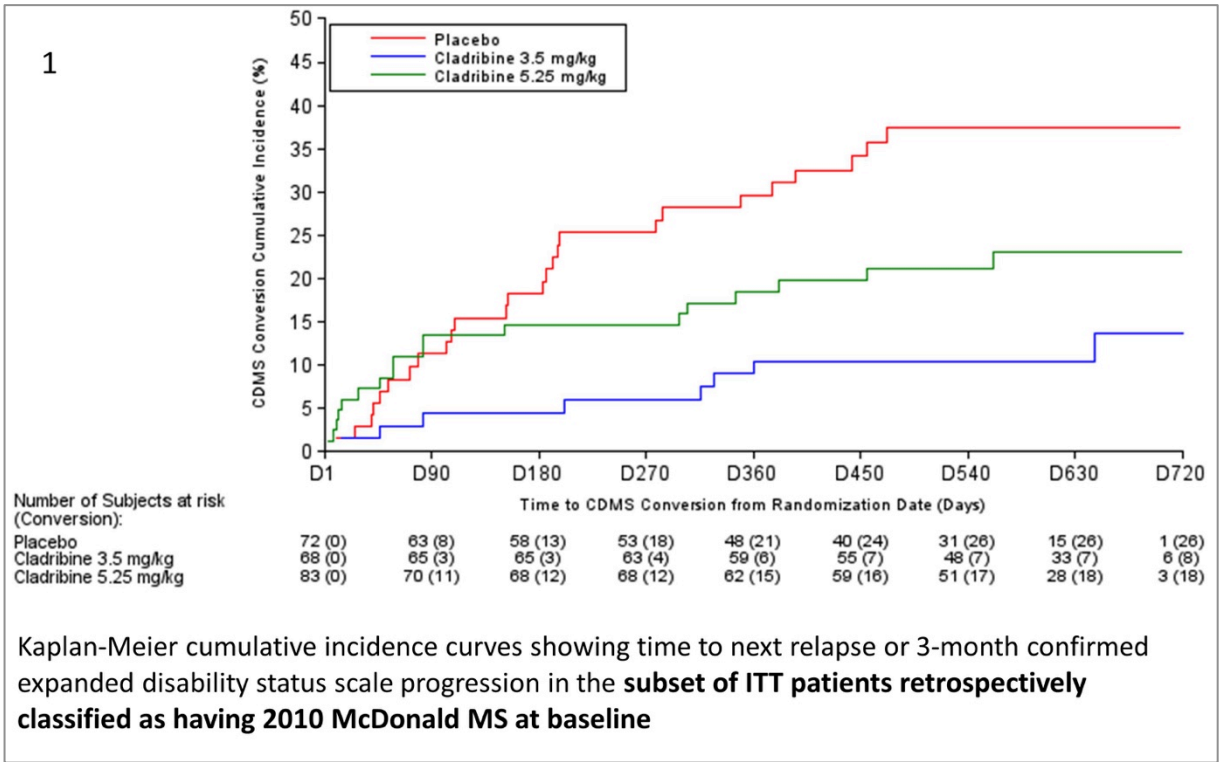


Fig. 1

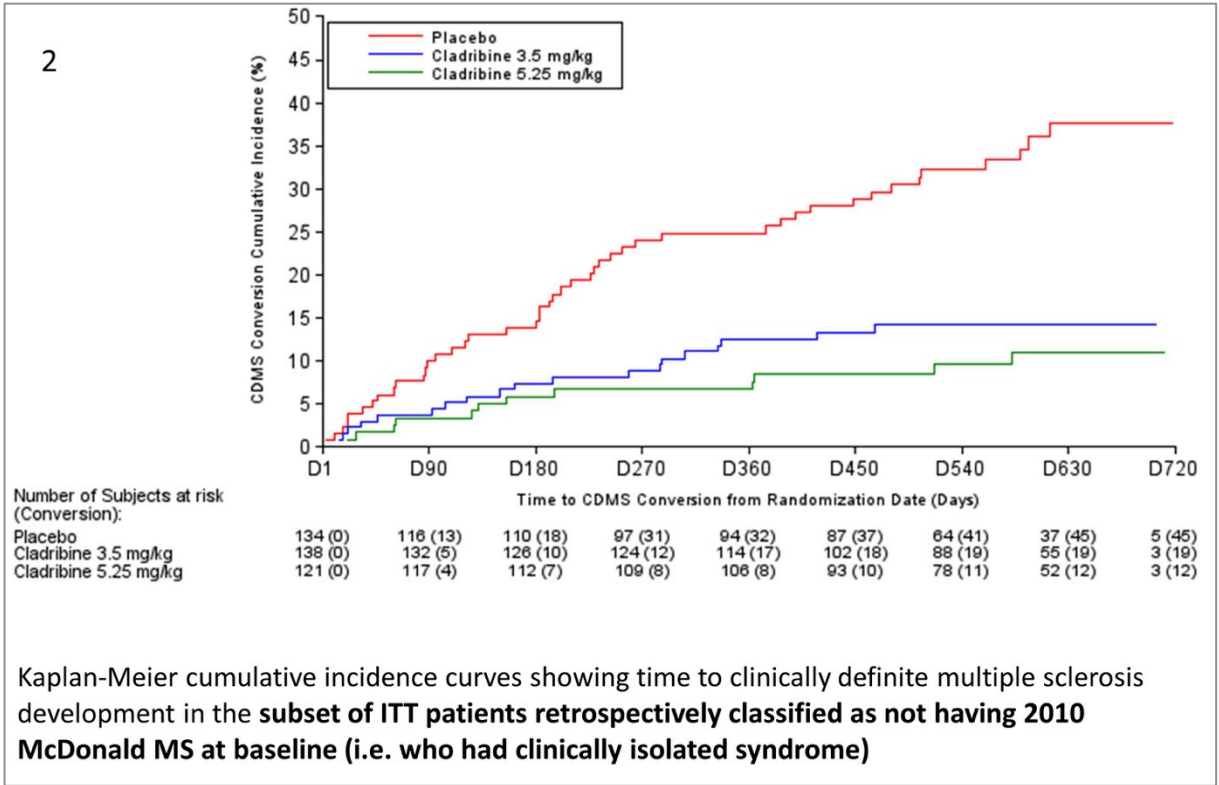


Fig. 2

P17**Magnetic resonance imaging (MRI) outcomes in patients with relapsing-remitting multiple sclerosis (RRMS) treated with cladribine tablets: results from the 120-week Phase IIIb extension of the CLARITY study**

G Comi [1], G Giovannoni [2], S Cook [3], P Rieckmann [4], K Rammohan [5], P Soelberg-Sørensen [6], P Vermersch [7], E Martin [8], F Dangond [8]

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Background

In CLARITY, cladribine significantly reduced relapse rates, MRI disease-activity measures and slowed disability progression. After a treatment gap (median 40 weeks), the effects of 2 additional years of cladribine treatment vs. placebo were investigated in CLARITY-Extension (EXT); MRI outcomes are described here.

Objective

To investigate the effects of cladribine on MRI disease activity measures in RRMS patients treated for 2 additional years beyond the initial 2-year regimen (CLARITY). **METHODS:** CLARITY patients were randomized to 2 years' treatment with placebo or cladribine (3.5 or 5.25mg/kg bodyweight). In CLARITY-EXT, placebo recipients in CLARITY received cladribine 3.5mg/kg; cladribine recipients were re-randomized 2:1 to cladribine 3.5mg/kg or placebo (5 groups total).

Results

The proportion of patients with no new T1 gadolinium enhanced (Gd+) lesions was 85.1–89.9% in cladribine-treated groups during CLARITY-EXT vs. 73.0–80.2% in placebo-treated groups. Respectively, the proportions with no active T2 lesions were 37.6–43.7% vs. 27.6–34.4%; proportions with no combined unique lesions were similar. Mean numbers of new T1 Gd+ lesions/subject/scan were 0.03–0.17 and 0.28–0.29, respectively, being significantly lower in patients treated with cladribine 3.5mg/kg in both CLARITY and CLARITY-EXT (0.03±0.08) vs. treatment with cladribine 3.5mg/kg in CLARITY and placebo in CLARITY-EXT (0.28±0.87, $P<0.001$). Of note, mean numbers of new T1 Gd+ lesions/subject/scan were <1 in 88.4% of patients in the latter group.

Conclusions

Overall, mean numbers of new T1 Gd+ lesions in CLARITY-EXT were low. Considering the favourable relapse-rate response seen in CLARITY-EXT, these findings suggest that the clinical benefits of 2 years' cladribine treatment were maintained for up to 4 years in the majority of patients. A small subgroup of patients treated with cladribine 3.5mg/kg in CLARITY and placebo in CLARITY-EXT showed some evidence of T1-Gd+ activity; decisions on further treatment could be based upon monitoring.

Study supported by Merck KGaA, Darmstadt, Germany.

P18**Safety and tolerability of cladribine tablets in patients with relapsing-remitting multiple sclerosis (RRMS): final results from the 120-week Phase IIIb extension trial to the CLARITY study**

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Background

In CLARITY, cladribine tablets significantly reduced relapse rates, disability progression and MRI measures of disease activity over 2 years. Consistent with cladribine's mechanism of action, the most commonly reported adverse event (AE) was lymphopenia. Patients who completed CLARITY entered a 2-year Extension (following a median gap of 40 weeks); those who completed CLARITY-Extension underwent safety monitoring for a further 6 months. Safety and tolerability outcomes were reported after 2 and 2.5 years.

Objective

To investigate safety (particularly, lymphocyte levels) and tolerability in RRMS patients in the 2-year CLARITY study and followed for 2.5 additional years on cladribine or placebo.

Methods

Patients who completed treatment in CLARITY were eligible for treatment in the Extension. Placebo-recipients in CLARITY received cladribine 3.5 mg/kg of body weight, while cladribine recipients (from the original 3.5 mg/kg or 5.25 mg/kg arms) were re-randomized 2:1 to cladribine 3.5 mg/kg or placebo for 2 years (5 groups in total).

Results

89 (11.0%) patients discontinued treatment due to AEs. Patients who transitioned from cladribine treatment to placebo during the Extension had fewer AE-related treatment discontinuations than those who continued on cladribine tablets. The incidences of lymphopenia and grade-3/4 lymphopenia were greatest in the groups receiving cladribine tablets in both CLARITY and the Extension; approximately 6% of patients receiving placebo in the Extension had a grade-3/4 lymphopenia. Most AEs were mild or moderate. The most common serious AEs in all groups were infections, gastrointestinal disorders and malignancies/unspecified tumours. Deaths (n=3) were considered unrelated/unlikely to be related to treatment.

Conclusions

Overall, safety and tolerability in CLARITY Extension were consistent with that seen in CLARITY.

Study supported by Merck KGaA, Darmstadt, Germany

P19**Clinical efficacy of cladribine tablets in patients with relapsing-remitting multiple sclerosis (RRMS): final results from the 120-week Phase IIIb extension trial to the CLARITY study**

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Background

Cladribine, given annually for 2 years in short-duration courses in CLARITY, significantly improved clinical (relapses and disability progression) and MRI outcomes. After a variable treatment gap (median 40 weeks), 2 additional years of cladribine treatment vs. placebo were assessed in CLARITY-Extension (EXT).

Objective

To assess efficacy of cladribine tablets in RRMS patients treated for 2 additional years beyond an initial 2-year regimen (CLARITY). **METHODS:** In CLARITY, patients were randomized to treatment with placebo or cladribine (3.5 or 5.25mg/kg bodyweight). In CLARITY-EXT, placebo recipients in CLARITY received cladribine 3.5mg/kg; cladribine recipients were re-randomized 2:1 to cladribine 3.5mg/kg or placebo (5 groups total). This allowed comparison of 2 years-only treatment plus ≥ 2 years follow up vs. 4 years' treatment. Clinical assessments included annualized relapse rate (ARR) and disability score.

Results

Baseline characteristics were similar across groups, although placebo-recipients in CLARITY showed evidence of greater clinical and MRI-disease activity. In groups treated with cladribine in CLARITY, efficacy was maintained in CLARITY-EXT; 2 years' additional-cladribine treatment was associated with a slight incremental benefit. The ARR in patients treated with cladribine 3.5mg/kg in CLARITY and placebo in CLARITY-EXT was 0.15 (97.5%CI 0.09–0.21; n=98); in patients treated with cladribine 3.5mg/kg in both CLARITY and CLARITY-EXT, ARR was 0.10 (97.5%CI 0.06–0.13; n=186, P=0.059). Both groups showed comparable proportions of relapse-free patients (75.6% and 81.2%, respectively) and times to first relapse (relative to first dose in CLARITY). Median EDSS scores were comparable across all groups; no significant between-group differences were seen in time to confirmed 3-month EDSS progression in CLARITY-EXT.

Conclusion

CLARITY-EXT demonstrated that in a majority of patients, the clinical benefits (relapse and disability) of cladribine 3.5mg/kg given in Years 1 and 2 may be maintained for at least 4 years, with decisions on further treatment based upon monitoring during this period. Study supported by Merck KGaA, Darmstadt, Germany

Study supported by Merck KGaA, Darmstadt, Germany

P20**Real-life long-term effectiveness of fingolimod in a Swiss relapsing-remitting multiple sclerosis cohort**

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Background

Fingolimod has been approved in Switzerland since January 2011 as the first oral treatment for relapsing-remitting multiple sclerosis (RRMS) to reduce frequency of relapses and delay disability progression. As opposite to the label granted by the European Medicines Agency, fingolimod has a first-line indication in Switzerland. With this study we wanted to assess the effectiveness of fingolimod in a real-world population that has been treated for up to 60 months with fingolimod

Methods

For this cross-sectional, retrospective study conducted in 19 centers in Switzerland, consecutive RRMS patients receiving fingolimod for a minimum of 7 and up to 58 months were included of whom demographic as well as clinical data were collected. The primary endpoint was number of patients being relapse-free. Key secondary endpoints included freedom of disability progression (EDSS score increase by ≥ 1 points) and treatment retention. All analyses have been performed using descriptive statistical methods including Wilcoxon- and paired t-tests as well (SAS® package, version 9.2 or higher).

Results

275 RRMS patients were included. Seventy-nine (28.7%) patients were treatment-naïve and the remaining 196 (71.3%) patients were switched from another therapy. Fingolimod treatment duration was <2 years in 75 (27.3%) patients, 2 to <3 years in 91 (33.1%) patients and ≥ 3 years in 109 (39.6%) patients. After a mean treatment duration of 32 months (range: 7 – 57.9 months) 214/275 (77.8%) [95% CI: 72.4%, 82.6%] patients were free from relapses. In addition, 244/270 (90.4%) [95% CI: 86.2%, 93.6%] patients were free from disability progression, and 195/270 (72.2%) [95% CI: 66.5%, 77.5%] patients were free from both relapses and disability progression. Treatment retention with fingolimod was 89.5%. Fingolimod was discontinued in 29 (10.5%) patients, of whom ten (3.6%) because of adverse events.

Conclusion

In this Swiss cohort of naïve and pre-treated RRMS subjects fingolimod treatment prevented the occurrence of relapses and disability progression in the majority of patients over 3 years. These findings support that fingolimod used in a real-life setting maintains the effectiveness shown over 2 years in the pivotal phase III trials.

P21**Teriflunomide in Routine Clinical Practice: Design and Baseline Characteristics of the TACO Study**

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Background

Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing–remitting MS (RRMS). Phase 3 studies of teriflunomide in patients with relapsing MS (TEMSO, NCT00134563; TOWER, NCT00751881) showed consistent efficacy across key clinical and magnetic resonance imaging (MRI) outcome measures (MRI assessed in TEMSO only), and a well-characterized safety profile. The phase 4 TACO study (Teriflunomide in RRMS patients Assessing Clinical benefit and patient-reported Outcomes in real-life medical practice) will monitor and evaluate patient-reported outcomes (PROs) assessed by clinical measurements and questionnaires in real-life medical practice in a Swiss RRMS cohort.

Objective

To describe baseline characteristics of patients enrolled in the TACO study.

Methods

TACO is a national, prospective, single-arm, multicenter, open-label study that evaluates PROs in patients with RRMS receiving teriflunomide 14 mg in Switzerland. The study duration is 24 months (12-month core study; 12-month extension follow-up) with target recruitment of 120 patients from 24 centers. The primary outcome is quality of life, measured by the validated Multiple Sclerosis Impact Scale (MSIS-29) questionnaire. Secondary outcome variables include relapses and disability worsening, as well as fatigue (measured by the FSMC scale), depression (HADS scale), cognition (MSNQ questionnaire), and treatment satisfaction (TSQM questionnaire). Safety and tolerability, adherence to safety monitoring, and health economic outcomes are also evaluated.

Results

As of April 15, 2016, 44 patients were enrolled in the study, the mean (standard deviation [SD]) age was 49.6 (10.9) years, and 60.5% of the patients were female. The mean (SD) time since first symptoms was 12.2 (7.6) years, and the mean (SD) baseline Expanded Disability Status Scale score was 2.4 (0.78).

Conclusions

TACO will provide valuable information on the current use of teriflunomide in the clinical setting, and will offer further insight into the use of PROs in patients with MS in routine clinical practice.

Study supported by Sanofi Genzyme.

P22**PET study of the nicotinic system in generalized and focal epilepsy**

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Introduction

Mutations of cholinergic neuronal nicotinic receptors (nAChRs) have been identified in a form of familial partial epilepsy, the autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). A PET imaging study using [18F] F-85380-A (18F-FA), an $\alpha 4\beta 2$ nicotinic receptor ligand, showed a significant uptake increase in the midbrain, pons and the cerebellum and a decrease in the right prefrontal dorsolateral region in these patients.

Aim

To evaluate if changes in the nicotinic receptors are observed in other epilepsy syndromes, given the neuromodulatory role of these receptors.

Methods

We included 34 participants, all male, 10 patients with non lesional diurnal focal epilepsy, 12 patients with idiopathic generalized epilepsy (IGE) and 12 age-matched healthy controls. Patients underwent PET imaging with 18F-FA, with 18F-Fluorodeoxyglucose and 3D T1 MRI for volumetric analyses. Binding potential (BP) 18F-FA parametric images using the corpus callosum as pseudo-reference region were calculated at 210-240 minutes post injection and compared with the control group using a voxel-wise analysis (SPM12) and a volume of interest (VOI) analysis.

Results

The SPM12 showed a significant ($p < 0.001$ uncorrected) increase of F-A-85380 uptake (corresponding to the receptor density) in the anterior cingulate cortex (ACC), bilaterally, in the group of patients with idiopathic generalized epilepsy (IGE). The VOI analysis ($p < 0.05$ uncorrected) confirmed a BP increase in the anterior cingulate cortex in the IGE patients and showed significant bilateral increase in the anterior cingulate cortex, as well as in the putamen, pallidum, and midbrain. In the group of patients with non lesional diurnal focal epilepsy, no significant increases or decreases have been observed, including the midbrain. Volumetric analysis did not show any significant volume change in the ACC in the group of IGE patients compared with the control group.

Discussion

We observed specific changes in the density/availability of nicotinic receptors in patients with IGE, different from the changes observed in ADNFLE and in the absence of changes in gray matter density in these regions. These data suggest that the modulation of $\alpha 4\beta 2$ receptors play a role not only in ADNFLE but also in other genetic syndromes, like IGE and may serve as biomarker of epilepsy syndromes with a genetic background.

P23**Efficacy and safety of fingolimod 0.5 mg every-other day in multiple sclerosis patients who presented severe adverse events when on conventional fingolimod treatment**

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Introduction

Fingolimod 0.5 mg every day (FTY-ED) is an approved treatment for relapsing-remitting multiple sclerosis. Reducing the frequency of FTY administration to every-other-day (FTY-EOD) has been suggested as a potential alternative to treatment discontinuation in case of severe adverse events, but efficacy and safety of this dosing schedule have not been investigated. We therefore analyzed the ability to prevent disease reactivation and the safety profile of FTY-EOD as compared to the approved FTY-ED dose.

Methods

This was a multicentre observational study including 60 consecutive FTY-EOD (mean follow-up 12.4 (7.6) months) and 63 FTY-ED (mean follow-up 22.9 (12.2) months) treated patients. Logistic regression was used to identify variables associated with a switch to FTY-EOD. Risk of disease reactivation (new relapses and/or increase in MRI lesion load) was assessed using Cox regression. Results were adjusted for baseline characteristics using propensity scores.

Results

The main reason to switch from FTY-ED to FTY-EOD was persistent lymphopenia and/or leucopenia (75% of patients), followed by increased liver enzymes (21.7%). Low weight was associated with a higher risk of being switched to FTY-EOD (OR=0.94, 95%CI=0.89-0.99, p=0.026), while female patients (OR=20.44, 95%CI=2.06-202.78, p=0.009) were more likely to be switched to FTY-EOD due to lymphopenia. The risk of developing relapses as well as either relapses or new demyelinating lesions on MRI was higher in FTY-EOD than FTY-ED (HR=3.27, 95%CI=1.27-8.44, p=0.014 and HR=2.19, 95%CI=1.17-4.09, p=0.014, respectively). Treatment with FTY-EOD increased lymphocyte count above 200/ul in the majority of lymphopenic patients (n=42, 93.3%). FTY-EOD was discontinued during the follow-up in 20 out of 60 patients, mostly because of insufficient efficacy (n=10) or persistent leuco-lymphopenia (n=4). No serious adverse events were observed during the study.

Conclusions

According to our multicenter observational study, reducing the administration of FTY to every-other day is safe, but also associated with an increased risk of disease reactivation.

P24

Brain FDG-PET analysis in patients suspected with Alzheimer's disease: comparison between computer-aided reading using SPM and BRASS.

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Visual analysis of FDG-PET hypometabolism mostly depends on reader's experience and there is no clear cut-off point between normal and pathological findings. To deal with these issues, automated software tools for computer-aided diagnosis have been developed, like SPM and Hermes BRASS™. Aim of this study is to evaluate and compare: 1) the extent and severity of the regional hypometabolism detected by SPMGrid (implementation of SPM8 into an online image analysis platform - www.neuGRID4you.eu) and BRASS, 2) the diagnostic properties of regional hypometabolism using two diagnostic categories: clinical and computer-aided diagnosis. This study included 41 healthy controls and 101 MCI patients from the EADC PET dataset. MCI patients were followed until conversion to dementia or for at least 36 months. Three independent expert readers expressed a diagnosis based on the pattern of hypometabolism detected by SPM and BRASS (normal, AD like, FTD like, LBD like, undetermined). The clinical diagnosis at follow-up (AD, DLB, FTD, HC, MCI stable) served as gold-standard. FDG-PET scans are voxel-wise analyzed for hypometabolism, by testing the single scan vs a control group of 106 healthy EADC PET subjects (SPM) or 3D reference templates created from images of 30 historical normal patients (BRASS). Results are provided by means of a 3D Students' t-map in the ICBM152 atlas space (SPM) or a 3D Gaussian z-map (BRASS) of the brain. Under the null hypothesis that the difference from the control group is voxel-wise equal to zero, the hypothesis of hypometabolism gets stronger as the t- (SPM) or z-value (BRASS) increases. Inter-reader agreement on diagnosis based over statistical maps was evaluated in terms of percentage agreement and kappa. Statistical values related to computer-aided diagnostic readings were compared to estimate their diagnostic validity. Inter-rater agreement was moderate for SPM (0.48) and fair for BRASS (0.36). The tools showed nearly equivalent AUC (0.67 for BRASS and 0.72 for SPM). BRASS showed higher sensitivity (82% vs 58%) and SPM higher specificity (87 % vs 52%). This study: 1) provides evidence of the validity of automated-assisted metabolic deficit detection in MCI subjects; 2) shows similar accuracy between BRASS and SPM, but also systematic differences in inter-rater agreement and diagnostic performance between the tools; 3) represent the basis to develop guidelines about the use of these automated tools in the diagnostic workup of AD patients.

P25**Positional nystagmus from BPPV in polysomnography of PD patients**

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Introduction

Patients with Parkinson Disease (PD) have an increased risk of falls due to postural instability, orthostatic dysregulation, or benign paroxysmal positional vertigo (BPPV). BPPV is common in PD, and BPPV often occurs during changes of head position in bed. We recently demonstrated that positional nystagmus can be discerned from other electrooculography (EOG) patterns. Since polysomnography is a commonly performed diagnostic test in PD, we aimed at elucidating the frequency of so-far undetected BPPV by analysis of EOG recordings.

Methods

Retrospective analysis of whole-night polysomnography recordings of 30 PD patients. EOG recordings were manually inspected and screened for nystagmus-like patterns. Patient characterization included disease duration, UPDRS III, and disease type. In addition, the impact of polysomnography variables on BPPV frequency was assessed.

Results

Twelve patients (40%) exhibited one or more nystagmus-like EOG episodes. Patients with and without nystagmus-like EOG episodes did not differ with respect to age (64 ± 11 y vs. 61 ± 8 y, $p=0.32$), UPDRS III (25 ± 9 vs. 23 ± 12 , $p=0.27$), or disease duration (9 ± 7 y vs. 7 ± 6 y, $p=0.42$). Sleep efficiency was similar between PD patients with and without nystagmus-like EOG episodes ($77\pm 14\%$ vs. $80\pm 15\%$, $p=0.53$).

Conclusion

Our preliminary findings indicate that BPPV may be more common in PD than appreciated so far, although the impact of nocturnal BPPV attacks on sleep quality remains unclear. The search for BPPV in polysomnography may be particularly meaningful in PD, as it has become a routine diagnostic tool in many specialized movement disorder units.

P26**Amyloid deposition in the muscle associated with ANO5-muscular dystrophy**

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Background

Muscle dystrophies associated with a recessive mutation of the anoctamin 5 (ANO5) gene were first described only a couple of years ago. ANO5 encodes a calcium-activated chloride channel belonging to the Anoctamin family of proteins. Mutations of this gene can result in proximal limb-girdle muscular dystrophy (LGMD2L) or distal non-dysferlin Miyoshi myopathy (MMD3); however, asymptomatic cases with elevated CK level have also been also reported. Histological examination of affected muscles reveals myopathic and dystrophic changes. Furthermore, amyloid deposits, previously known to be associated with dysferlinopathy, might also be rarely present, suggesting some similarities between the two muscle dystrophies.

Aim

We present a patient with an ANO5-associated limb-girdle muscular dystrophy, in whom muscle biopsy revealed perivascular amyloid deposits in the absence of evidence for systemic amyloidosis.

Results

We report a 47 year-old patient with a history of back pain since his late twenties and weakness of his left leg with walking disturbances as well as pain of the hips during physical activity starting at the age of 42. Clinical examination showed atrophy of the lumbar paravertebral and ischiocrural musculature with symmetrical proximal weakness of the legs. CK was elevated to 32-fold of reference. Muscle biopsy revealed myopathic changes and perivascular amyloid deposits. Other causes of amyloidosis, including dysferlinopathy, were ruled out. Skin biopsy did not show signs of systemic amyloidosis and cardiac check-up was normal. Genetic testing of ANO5 confirmed compound heterozygosity and the novel mutation c.1922G>A (exon 18) which is predicted to be probably pathogenic.

Conclusion

ANO5-associated muscle dystrophy is a heterogeneous predominantly adult onset disorder with similarities to dysferlinopathies. Amyloid deposits in the muscle can occur and may give a diagnostic hint, although their protein composition remains elusive. While our patient did not show cardiac involvement, cardiomyopathy and cardiac arrhythmia can be associated with ANO-5 mutations.

P27**Validation of an automated lateral ventricle delineation algorithm (ALVIN) in multiple sclerosis**

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Background

ALVIN is an algorithm for the automated lateral ventricle segmentation in SPM8 that has been primarily validated in Alzheimer's disease.

Objective

To assess scan re-scan reliability, the correlation between ALVIN and manual segmentation and the effect of lesion-filling on the association between lateral ventricle volume(LVV) and disability in multiple sclerosis (MS).

Methods

High resolution 3D T1 MPRAGE images were acquired on a 1.5T MRI system from 132 MS patients(75% relapsing-remitting MS; 66% female, mean age 44.4 ± 10.6 and disease duration 13.1 ± 9.1 years) with follow-ups at 3 and 5 years. T1 hypointense lesions were filled using FSL. ALVIN applies a binary mask to spatially normalized CSF segmented images using the unified segmentation option in SPM8 and calculates the normalized LVV. Scan re-scan reliability was assessed in 17 healthy controls(HCs) re-scanned immediately after the first scan in the same scanner. Manual segmentation of the LV was performed in 45/132 patients. The association between ALVIN and manual segmentation was assessed using the intraclass correlation coefficients(ICC) and Bland Altman limits of agreements. To assess disability we used the EDSS, MSFC and SDMT. Associations between LVV and clinical outcomes were investigated using Spearman correlations and further explored using linear regression models. Akaike information criterion was used to compare the goodness-of-fit between linear regression models.

Results

Scan re-scan reliability was high(ICC=0.99) with a mean LVV difference between the two scans of 0.007 ± 0.273 ml(95% CI:-0.542 ml; 0.528 ml). In patients, the mean LVV at baseline using ALVIN was 29.8 ± 14.3 ml. The agreement between ALVIN and manual segmentation was high(ICC=0.986). ALVIN tended to overestimate the LVV with a mean difference of 0.91 ± 1.55 ml compared to the manual segmentation. At baseline, the volume of hypointense MS lesions on T1-weighted images was 2.4 ± 3.6 ml and had influence on the ALVIN. LVV was lower when ALVIN used lesion-filled compared to non-lesion filled images with a mean difference of 0.41 ± 0.68 , 0.30 ± 0.61 and 0.41 ± 0.62 ml at baseline, 3 and 5 years, respectively(all $p < 0.001$). When using lesion-filled images, the associations between LVV and clinical outcomes were closer compared to lesion-unfilled images.

Conclusion

Scan re-scan reliability of ALVIN in HCs is high. ALVIN correlates with manual segmentation in MS. ALVIN overestimates the LVV when lesion-unfilled images are used.

P28**Lateral Ventricle Volume change is associated with neurological and cognitive disability in multiple sclerosis: a 5-years follow-up study using an automated lateral ventricle segmentation algorithm**

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Background

As pars pro toto, the lateral ventricle volume (LVV) might give an indirect estimate of brain volume (BV). ALVIN (automatic lateral ventricle delineation) is an algorithm that has been primarily validated in Alzheimer's disease and segments the LV from structural MRI. Objectives: To investigate the association between LVV and disability in multiple sclerosis (MS) longitudinally.

Methods

High-resolution 3D T1 MPRAGE MRI data with 3 and 5 years follow-up were derived from a longitudinal MS cohort. T1 hypointense lesions were marked using Amira (Mercury Computer Systems Inc.) and filled using FMRIB Software Library. ALVIN applies a binary mask to spatially normalized CSF segmented images using the unified segmentation option in SPM8 and calculates the normalized LVV. Neurological and cognitive disability was assessed using the Expanded Disability Status Scale (EDSS), Multiple Sclerosis Functional Composite (MSFC) and Symbol Digit Modalities Test (SDMT). Associations between LVV and clinical outcomes were investigated using Spearman correlation. Sample size calculation was based on two group t-test for differences between independent means. For comparison, normalized (N)BV was calculated using Sienax.

Results

In total, 132 patients were included: 76% relapsing-remitting (RR)MS, 66% female, mean age 44.4 ± 10.6 and disease duration 13.1 ± 9.1 years, median EDSS 3.0 (range 0-6.5). At baseline, mean LVV was 29.8 ± 14.3 ml and correlated with age ($\rho=0.24$; $p=0.006$), disease duration ($\rho=0.38$; $p<0.001$), T1 lesion volume ($\rho=0.56$, $p<0.001$), T2 lesion volume ($\rho=0.56$, $p<0.001$) and NBV ($\rho=-0.57$; $p<0.001$). Mean LVV was higher in progressive MS than clinically isolated syndrome or RRMS ($p<0.001$). However, this difference did not remain significant when adjusted for age and gender ($p=0.07$). The mean LVV increased by 3.6 ± 4.6 ml over 5 years corresponding to a mean annual LVV change of 0.7 ml (2.3%). Mean LVV change was marginally higher in men than women ($p=0.06$). LVV correlated with EDSS, MSFC and SDMT at all time-points ($\rho=0.34-0.47$; all $p<0.001$). Based on LVV changes observed, in future trials, sample size calculation estimates 126 patients in each treatment arm required to detect a 50% difference in LVV change over 3 years (80% power, $\alpha=0.05$).

Conclusions

The LVV measured using ALVIN correlated with NBV assessed using SIENAX and with neurological and cognitive disability in MS.

P29**Deregulation of the proteostasis network in diseased muscle.**

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Muscle wasting originates from the pathological deregulation of myofibrillar proteostasis. This process is mainly driven by the Foxo-dependent activation of the Atro-genes, genes that encode for intermediates of the ubiquitin-proteasome and the phago-lysosome degradation machinery. Expression of Fbxo32, also known as Muscle Atrophy F-box (MAFbx) or Atrogin1, is an E3 ligase-associated Fbox protein is dramatically induced in response to atrophic signals and to activities that trigger ubiquitin-dependent muscle breakdown^{1,2}. To date, the molecular mechanism involved in the activation of Fbxo32-associated E3 ligase remains poorly understood. We combined molecular and cell biological techniques to identify the domains important for its function for the regulation of its activity. The generation of various deletion mutants and their expression in proliferating and differentiated muscle cells allowed us to precisely map the Fbxo32 domains required for its correct subcellular distribution. We already demonstrated that the amino-terminal region of Fbxo32 (aa 1-180) which encodes one of the two functional nuclear localization signal (NLS) found in Fbxo32 contains two additional motifs (Leucine Zipper (LZ) and Leucine charged domain (LCD) which we are involved in substrate recognition and binding^{3,4}. Here we show that this amino-terminal region of Fbxo32 also interacts with the tetratricopeptide (TPR) repeat containing protein 7 (TTC7). We further show the molecular interaction between this TPR rich protein, the Fbxo32-associated E3 ligase complex and its known substrates EIF3F and MyoD^{3,4}. We propose a working model where this adaptor functions as a scaffold for Fbxo32-associated E3 ligase activation.

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P30**Identification of Plant-derived Alkaloids with Therapeutic Potential for Myotonic Dystrophy Type I**

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Myotonic dystrophy type I (DM1) is a disabling neuromuscular disease with no causal treatment available. This disease is caused by expanded CTG trinucleotide repeats in the 3' UTR of the dystrophin protein kinase gene. On the RNA level expanded (CUG)_n repeats form hairpin structures that sequester splicing-factors, such as muscleblind-like 1 (MBNL1). Lack of available MBNL1 leads to mis-regulated alternative splicing of many target pre-mRNAs, leading to the multisystemic symptoms in DM1. Many studies aiming to identify small molecules that target the (CUG)_n-MBNL1 complex focused on synthetic molecules. In an effort to identify new small molecules that liberate sequestered MBNL1 from (CUG)_n RNA we focused specifically on small molecules of natural origin. Natural products remain an important source for drugs and play a significant role in providing novel leads and pharmacophores for medicinal chemistry. In a new DM1 mechanism-based biochemical assay, we screened a collection of isolated natural compounds, and a library of over 2100 extracts from plants and fungal strains. HPLC-based activity profiling in combination with spectroscopic methods were used to identify the active principles in the extracts. Bioactivity of the identified compounds was investigated in a human cell model and in a mouse model of DM1. We identified several alkaloids, including the beta-carboline harmine and the isoquinoline berberine, which ameliorated certain aspects of the DM1 pathology in these models. Alkaloids as a compound class may have potential for drug discovery in other RNA-mediated diseases.

P31**Development of aptamers for DUX4 transcription factor - a potential therapeutic target in Facioscapulohumeral muscular dystrophy**

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Facioscapulohumeral muscular dystrophy (FSHD) is the third most common muscular dystrophy which is estimated to affect around 12 in every 100,000 individuals¹. The disease is characterized by muscle weakness in the facial scapula and upper arm regions of the body. Currently there are no FDA approved treatments for FSHD but one strategy being developed includes the use of RNAi to silence the DUX4 gene. Since the identification of the DUX4 gene activation and translation of DUX4 transcription factor the possibility to develop inhibitors as a therapeutic agent in the treatment of FSHD has become a reality. Aptamers are short oligonucleotides consisting of either ssDNA or RNA which bind to a variety of different biomolecules such as proteins small molecules and whole cells.

Since the first aptamer based drug (pegatanib) was approved for the treatment of neovascular age related macular degeneration, the potential for aptamers to be used as therapeutic agents has been realised and currently there are at least ten aptamer candidates undergoing clinical trials.

In this project, we successfully selected aptamers for DUX4 transcription factor using a modified SELEX procedure and identified that the ssDNA aptamers found shared a common binding motif with the PITX1 promotor region.

We demonstrated a successful strategy for selecting aptamers against a transcription factor expressed with two affinity tags.

We also demonstrated the use of qPCR and next generation sequencing in the SELEX procedure. To the best of our knowledge, ssDNA aptamers for DUX4 have not previously been reported.

P32**The European Prevention of Alzheimer's Dementia (EPAD/AMYPAD) projects: the Swiss contribution.**

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Background

Approximately 110,000 people are estimated to be living with dementia in Switzerland, most of whom have Alzheimer's disease (AD). About twice as many have milder degrees of cognitive impairment and are at high risk of developing dementia after a few years. The purpose of the European Prevention of Alzheimer's Dementia (EPAD) project (www.ep-ad.org) is to test disease-modifying drugs aimed to prevent Alzheimer's dementia in non-demented at-risk persons, by acting on the underlying molecular biology (amyloid and tau deposition).

Methods

EPAD project is establishing a European-wide register of 24,000 participants, of which 6,000 people - 700 from Switzerland - will be asked to join a pan-European longitudinal cohort study (LCS) for serial deep phenotyping with AD biomarkers. The EPAD LCS will start in April 2016. Approximately, 1,500 of the participants from the EPAD LCS will be invited to enter the EPAD trials with disease modifiers starting from 2nd quarter 2017. Disease modifiers to be tested are currently being identified.

Results

As of April 2016, three cohorts have initiated the process to join the EPAD registry, representing approximately 12,000 potential research participants: the memory clinic-based Epinettes (Consultations de la Mémoire, Geneva University Hospitals), Clemens (Centre Leenaards de la Mémoire, Centre Hospitalier Universitaire Vaudois) and the population-based Bus Santé study (Geneva University Hospitals). As of the time of submission of this abstract, activities are ongoing to secure the participation of subjects from the academic memory clinics of Zurich, Bern and Basel.

Conclusions

The EPAD initiative will allow Switzerland to take part to the paradigm shifting approach of preventing Alzheimer's disease. The long-term vision wants Alzheimer's to become a preventable disease, as it was the case of stroke decades ago.

This work has received support from the EU/EFPIA Innovative Medicines Initiative Joint Undertaking EPAD grant agreement n° 115736

P33**Abcg2-expression during experimental autoimmune encephalomyelitis and its functional impact on Teriflunomide treatment in vitro and in vivo**

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Background

The multi-drug resistance transporter Abcg2, a member of the ATP-binding cassette (ABC) family, mediates the efflux of xenobiotics across cell membranes and organelles. Different immunotherapeutics used in Multiple Sclerosis (MS), e.g. teriflunomide (teri) and mitoxantrone are known substrates of Abcg2. Characterization of potential regulation of Abcg2 activity and function during chronic neuroinflammatory disease could help to optimize treatment strategies.

Objective

To investigate abcg2-transporter expression during experimental autoimmune encephalomyelitis (EAE) and its functional impact on teri-treatment in vitro and in vivo. Methods Quantitative rtPCR for abcg2-transporter mRNA expression was performed on spinal cord, brain, liver and spleen of C57Bl6 wild-type (WT) mice during chronic MOG35-55 EAE (baseline (BL) vs. peak (ac) or chronic (chr) phase). Stimulated T-cells (anti-CD3, 10µg/ml; anti-CD28, 10ng/ml; 24h or 48h) from WT and abcg2-KO were treated with teri (12.5-100µM) +/-abcg2-inhibitor fumitremorginC (10µM; FTC). T-cell death (annexinV/PI) and proliferation (CFSE) were analyzed by flow cytometry. Chronic EAE was induced by active immunization with MOG35-55 in WT and abcg2-KO. Teri (10 mg/kg b.w.) was given orally once daily after individual disease onset.

Results

During different phases of EAE and within the CNS, abcg2 is differentially regulated. In spinal cord it decreases during acute and increases during chronic phase (BL vs. ac: 5x decreased; BL vs. chr: 4x increased) whereas it is contrary regulated in the brain (BL vs. ac: 3x increased; BL vs. chr: 3x decreased). During chronic phase, abcg2-expression was decreased in liver (2x, p=0.009) but unchanged in spleen. In vitro, teri-induced inhibition of T-cell proliferation in WT cells was strongly dose-dependent (p<0.01) and was significantly increased by FTC (p<0.05 for teri 25, 100µM). T-cell apoptosis was significantly increased in abcg2-KO cells compared to WT (p<0.05 for teri 12.5-50 µM). In vivo, teri-treatment ameliorated clinical EAE-course more pronounced in abcg2-KO than in WT.

Conclusions

EAE-induced inflammatory conditions modulate abcg2-expression differentially in the CNS and the periphery. Functional relevance of abcg2 on teri in vitro is indicated by increased teri-induced inhibition of T-cell proliferation by FTC and by increased T-cell apoptosis in abcg2-KO T-cells. In vivo relevance is indicated by a stronger therapeutic effect in abcg2-KO mice than in WT.

This study is funded by Genzyme.

P34

Quantitative EEG and Verbal Fluency in Patients with Parkinson's Disease and STN-DBS

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Introduction

Verbal fluency is known to decline after deep brain stimulation in the subthalamic nucleus (STN-DBS, Wyman-Chick 2016). The decline of verbal fluency after STN-DBS is hypothesized to arise from striatal dysfunction (De Gaspari 2006). It is still unknown whether this decline is mainly due to the surgical lesion or to the electrical stimulation. Here we compare verbal fluency and quantitative EEG measures in the stimulator on/off condition.

Methods

7 patients with STN-DBS were included in the still ongoing trial. All patients had a high density EEG recording in the stimulator on/off situation, while the phonemic, semantic, alternating phonemic and semantic verbal fluency was tested (Regensburger Wortflüssigkeits-Test). Stimulus artifact was suppressed by a combination of filtering, principal and independent component analysis.

Results

The frequency analysis showed an increase of absolute delta, theta and beta power in the stimulation ON condition as compared to the stimulation OFF condition ($p \leq 0.01$). Semantic fluency showed a non-significant trend towards a decrease in the OFF condition ($p = 0.3$).

Conclusion

The increase of beta-power in resting state EEG, especially in the paracentral regions, may represent partial normalization at least in the motor (Weiss 2015, Oswal 2016) and possibly in other cortico-basal-thalamic loops and is in concordance with earlier reports. In contrast, the increase of delta- and theta-power may be explained by an aliasing effect and doesn't necessarily represent alteration of brain function. The trend towards an increase of semantic verbal fluency might be related to improved cognitive flexibility (Witt 2004, Koerts 2013).

P35**Real-world data on the management of patients with multifocal motor neuropathy (MMN) or chronic inflammatory demyelinating polyneuropathy (CIDP) with immunoglobulins: long-term data of the SIGNS study**

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Background and aim

The management of patients with neurological autoimmune diseases under real-life conditions has only insufficiently been elucidated. We aimed to collect observational data on patients with chronic inflammatory demyelinating polyneuropathy (CIDP) or multifocal motor neuropathy (MMN) who receive intravenous (IV) or subcutaneous (SC) immunoglobulins (IG) as maintenance therapy to improve muscle strength.

Methods

Prospective, non-interventional study (registry) in neurological centres (hospitals and offices) across Germany.

Results

As of 03 April 2016, 81 patients with MMN (mean age 44.6 ± 11.7 years, 68% males, mean disease duration 10.7 ± 10.1 years) and 53 patients with CIDP (53.4 ± 13.1 years, 66% males, 7.1 ± 5.6 years disease duration) were included. On MRC, MMN patients had in 3.1% normal strength, in 24.6% limitations of grade 4 and in 72.3% of grade 0-3; of the CIDP patients 31.0% had normal strength, 37.9% grade 4 and 31.1% grade 0-3. With regard to the INCAT score (indicating disability) of the CIDP patients 31% had no limitations in the arms and 25% none in the legs, of the MMN patients 5% none in the arms and 40% none in the legs. On average patients received IV IG with a mean monthly dosage of 0.9 g/kg (MMN) and 0.6 g/kg (CIDP) body weight, with substantial variations between patients, but not over time. At 1 year, the majority of patients remained clinically stable as assessed by MRC and INCAT scores. Quality of life improved as measured with Short Form-36 and other instruments.

Conclusions

There is a wide dose range for the treatment of patients with MMN or CIDP with variations in both single doses and treatment intervals. Muscle strength and reduction in disability improved or remained at least stable in the great majority of patients, accompanied by increased quality of life, which further strengthens the use of IG as maintenance treatment in MMN and CIDP.

The study was funded by Baxalta, Germany and USA.

P36**Acute clinical deterioration of a patient with spinal dural arteriovenous malformation after lumbar puncture and steroid treatment – a case report and discussion of possible reasons**

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Introduction

Spinal dural arteriovenous malformations are rare causes of subacute onset of progressive spinal symptoms including paraparesis, sensory deficits, sphincter and bladder disturbances and back pain. The pathophysiology of a spinal dural arteriovenous fistula (SDAVF) is venous hypertension and a decrease of arterial supply of the spinal cord causing venous congestion and therefore leading to progressive necrotizing myelopathy. Neurosurgical or interventional treatment is required as soon as possible.

Case description and disease course

We present a 56 year-old women with a 3 weeks history of bladder and bowel sphincter dysfunction, progressive parapareses and muscle pain in both legs. Lumbar puncture was performed to exclude an infectious or immunologic etiology for the white matter alterations seen in the MRI longspine. Also a high-dose steroid treatment was initiated. Some hours later an acute deterioration occurred and the patient developed paraplegia of the lower extremities. Finally the diagnosis of a SDAVF was made the day after and neurosurgical treatment was initiated immediately.

Discussion

There are descriptions in the literature about deterioration of SDAVFs following lumbar puncture directly after penetrating the dura, which was not the case in our patient. It is known that steroid treatment can cause a deterioration in these patients too, but the pathophysiology behind is not completely understood.

Conclusion

We want to increase awareness of this rare but treatable cause of subacute progressive myelopathy as an important differential diagnosis.

- We suggest not to perform a lumbar puncture in patients suspicious for SDAVF.
- The impact of steroid treatment in SDAVF patients is unclear but is probably better to be avoided.

P37**One unexpected increase in clinical and MRI disease activity after first course of Alemtuzumab besides many positive outcomes**

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Alemtuzumab is a humanized monoclonal antibody directed against CD52. It is approved for treating active relapsing multiple sclerosis (RRMS) and has been shown to reduce relapse rate and sustained accumulation of disability in patients with active or first-line treatment-refractory MS. To describe clinical and MRI disease activity after first course of alemtuzumab in patient with highly active RRMS non-responsive to first-line treatments. We report on a 29-year-old, JCV positive male diagnosed with RRMS in 2011. He started his therapy with interferon beta-1a (3x44µg) and switched due to high disease activity to fingolimod 6 months later. Because of ongoing disease activity under fingolimod, dimethylfumarate (DMF) was introduced in October 2014. However, he still experienced high clinical (3 relapses) and radiological (new Gd+-enhancing lesions) disease activity, leading to a decision to stop therapy with DMF in February 2015 do to our positive experience with Alemtuzumab switching to it. The first alemtuzumab course (12 mg/day on 5 consecutive days) was infused in April 2015. Surprisingly, in the following months disease activity increased. The Patient experienced several relapses and his MRI in September 2015 demonstrated new and active cerebral and spinal lesions. A control MRI in January 2016 showed ongoing radiological activity with more than 30 smaller Gd+-enhancing lesions. We decided to treat the patient with rituximab instead of the previously planned second course of alemtuzumab. In our patient with highly active RRMS refractory to first-line treatment options the clinical and MRI activity surprisingly increased after first course of alemtuzumab. This is in contrast to the literature and our previous practical experience with this substance. We hypothesize that a robust lymphocyte repopulation may be responsible for this unexpected reaction. Recovery of T and B cell populations occurs with different kinetics, B cells returning much earlier (1-2 months) in peripheral blood (Hartung et al 2015). This may explain the increase in the disease activity in some MS patients with a probably "B cell dominated MS". To our knowledge, there are several personal communications, reporting insufficient response or even increased disease activity after alemtuzumab treatment in some patients. Interestingly, on a B-cell depleting rituximab therapy disease activity seemed to decrease in all those patient who did not respond to alemtuzumab therapy.

P38**Added value of combined semi-quantitative and visual 123I-FP-CIT SPECT analyses for the diagnosis of dementia with Lewy bodies**

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Introduction

To assess the validity of a semi-quantitative 123I-FP-CIT SPECT method, compared to the commonly used visual analysis, in patients with probable dementia with Lewy bodies (DLB) and Alzheimer's disease (AD). We also studied DLB specific uptake impairment pattern and correlation of uptake in the presence or absence of parkinsonism.

Methods

among 1'202 scans performed at our center from 2003 to 2015, we identified 93 subjects with probable DLB (mean age 76.9 ± 6.8 year, 47% women) and 18 with AD (mean age 76.9 ± 8.1 year, 50% women). Independent visual and semi-quantitative assessments based on previously established on-site reference values (including volumes-of-interest uptake, caudate-to-putamen ratio and striatal asymmetry index) were performed and compared between both groups.

Results

Visual staging was considered abnormal in 96.8% of DLB patients, whereas 97.8% of subjects had an abnormal semi-quantitative assessment. Combining both methods yielded a 100% sensitivity. Patients with DLB exhibited a more pronounced impairment of putaminal uptake when associated with parkinsonism, whereas a more diffuse pattern and significantly higher uptake values were observed in the subgroup of DLB patients without parkinsonism (resp. striatal uptake 1.61 ± 0.66 vs 2.28 ± 0.52 , $p=0.01$). A minority of AD subjects show minimal alterations of presynaptic dopaminergic transport (striatal uptake 3.07 ± 0.41), values being always significantly higher than those from DLB patients, irrespective of the presence of parkinsonism ($p<0.0001$) or not ($p=0.002$) in the DLB population.

Conclusions

Additional use of semi-quantitative analysis allows a higher discrimination of DLB from AD and demonstrates a specific pattern of degeneration in DLB patients according to their motor phenotype.

P39**Roadmap to the Biomarker-Based Diagnosis of Alzheimer's Disease**

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Background

The diagnosis of Alzheimer's disease (AD) is shifting from a clinical-pathological to a clinical-biological paradigm. Biomarkers (BMs) of Alzheimer's pathology have good analytical validity, but incomplete clinical validity and utility. A coordinated effort to validate AD biomarkers is needed for their implementation in the clinic and for reimbursement. Objectives An international task force (experts on AD and cancer biomarkers, scientific societies, patient advocates, and regulators) set out to identify the gaps of evidence to full clinical validity of AD BMs and define actions into a coherent and cost-effective roadmap.

Methods

The task force adapted a framework for BMs development used in oncology to AD including five logically sequential phases: pilot studies on analytical validity, assay development for clinical disease, prospective longitudinal repository studies, prospective diagnostic studies, and disease control studies. We assessed existing evidence based on this framework for amyloid-PET; CSF Aβ42, tau/phospho-tau; FDG-PET; hippocampal atrophy, 123I-Ioflupane, 123I-MIBG, and neuropsychology.

Results

Our reviews show robust evidence for Phase 1 for all BMs. Phases 2 and 3 have been addressed inconsistently. Only preliminary evidence is available for some Phase 4 aims for amyloid-PET, CSF biomarkers, hippocampal atrophy, and FDG PET. Phase 5 has not yet been addressed. Compared to other BMs, hippocampal atrophy and FDG-PET are at a relatively advanced stage of validation, while neuropsychology, 123I-ioflupane and 123I-MIBG validity studies are relatively less advanced (Table 1). The conduction of future studies in the context of a broadly accepted framework is warranted to fill the existing gaps. We propose the following development and validation scheme (Figure 1) where phases 2 and 3 should be completed before moving to phases 4 and 5 in realistic patients and settings: definition of guidelines for the clinical use of BMs, qualification of memory clinics for BMs, centralized/harmonized strategies for their assessment, and a national plan to allow equitable access to BMs.

Conclusions

This exercise identified gaps that should be addressed to accelerate AD biomarker implementation in the clinic. The roadmap is intended for policy makers, private and public funders of clinical research and pharma, researchers, and scientific societies. Figure 2 shows the decision nodes where the roadmap can be used.

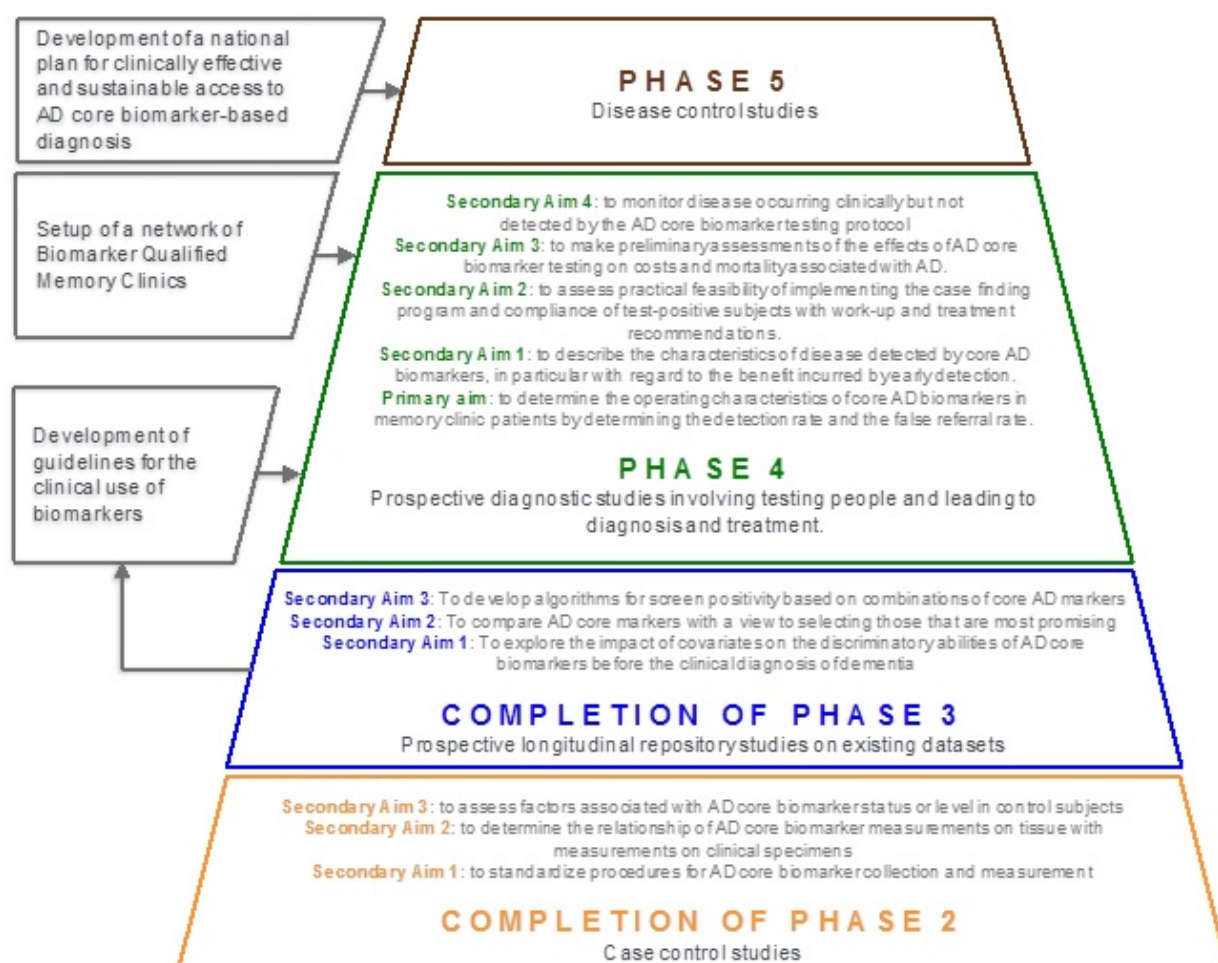


Fig. 1

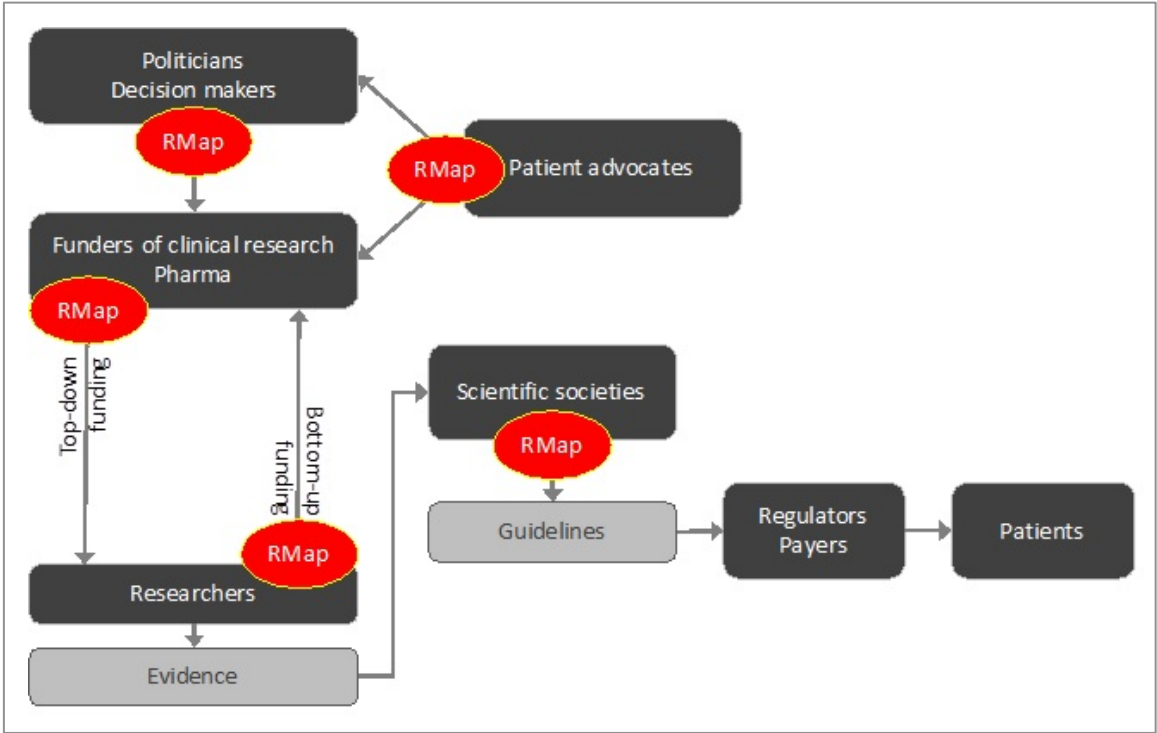


Fig. 2

Table 1

Biomarker	Phase I Pilot Studies	Phase II Clinical Assay Development for Clinical Disease						Phase III Prospective Longitudinal Repository Studies						Phase IV Prospective Diagnostic Studies					Phase V Disease Control Studies			
	PA 1	PA	SA 1	SA 2	SA 3	SA 4	PA 1	PA 2	SA 1	SA 2	SA 3	SA 4	PA	SA 1	SA 2	SA 3	SA 4	PA	SA 1	SA 2	SA 3	
Neuropsychology																						
CSF																						
Amyloid PET																						
FDG PET																						
Tau PET																						
Hippocampal atrophy on MR																						
123I-ioflupane SPECT																						
123I-MIBG SPECT																						

Achievement

Full

Partial

Preliminary

Not Achieved

Not Applicable

P40**Temporomandibular joint disorder in comorbidity with trigeminal neuralgia or persistent idiopathic facial pain**

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Aim

The aim of this study was to evaluate accurate differentiating between the temporomandibular joint (TMJ) disorder with idiopathic trigeminal neuralgia (TN) and persistent idiopathic facial pain (PIFP) in the sample of patients from a subspecialist dental practice.

Methods

All 36 patients (35 female) were previously neurologically examined due to unconfirmed suspicions of a neurological origin of orofacial pain. TMJ-disorder was diagnosed by using the Diagnostic Criteria for Temporomandibular Disorders and the diagnosis was confirmed by using magnetic resonance imaging. The study included 18 patients (group G-1, mean age 59.6 years, 17 female) with TMJ disorder and TN, and 18 patients (group G-2, mean age 52.9 years, all female) with TMJ disorder and PIFP. Clinical characteristics, pain intensity related to TMJs and neurological disorder (TN or PIFP) rated on a visual-analogue scale (VAS with range 0-10).

Results

There was no significant difference between TMJ pain on the VAS scale for G-1 patients with 6.1 and for G-2 patients with 6.2 ($p > 0.05$). However, there was a statistically significant difference in the intensity of TN and PIFP related pain ($p < 0.001$) for G-1 patients (pain on VAS was 9.8) and for G-2 patients (pain on VAS was 4.0). In group G-1 with TN, flashing pain was dominant in 77.8% of the patients and 22.2% suffered from stabbing pain. Patients with PIFP (G-2) mostly suffered from a tingling sensation (61.1%), numbing pain (16.6%), pulsating sensation in the face (11.1%) as well as from burning sensation and swelling 5.6% each. The triggering stimuli are dominant in 61.1% of patients with TN, whereas in patients with PIFP they occur rarely (11.1%). In G-1 group, 55.5% of the patients have undergone various dental procedures, and only 11.1% of patients from the G-2 group. All the patients with TN had localized paroxysmal attacks, whereas in patients with PIFP, 72.2% of them had long-term diffuse pain and the other 27.8% had long-term localized pain. The ophthalmic branch was the least involved (16.6% of patients).

Conclusions

In the diagnostic process of TMJ-pain, neuropathic pain disorders (TN and PIFP) make the diagnostics of musculoskeletal pain in the orofacial region difficult. Correct diagnosis is the key to managing facial pain of non-dental origin, which includes participation of several experts from the fields of dental medicine, neurology and radiology.

P41**White matter changes in normal pressure hydrocephalus**

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Aims

White matter changes (WMC) are common in patients with idiopathic normal pressure hydrocephalus (iNPH), however it is unclear if WMC may differentiate patients with iNPH from similar neurological condition (iNPH mimics). This cross-sectional study aims to determine if WMC can identify patients with iNPH from its mimics and evaluate if WMC are associated with clinical symptoms (gait, cognition and urinary disturbances).

Methods

One hundred and forty-one consecutive patients (75.7 ± 7.1 years; 31.2% women) with a suspicion of iNPH (79 iNPH and 62 iNPH mimics) were included in this analysis. WMC were measured with the age-related white matter changes scale (ARWMC – range 0-30) and clinical symptoms were assessed with the iNPH grading scale. Covariates included age, gender and parkinsonism.

Results

The mean ARWMC was similar between patients with iNPH and iNPH mimics (5.33 ± 4.21 and 5.53 ± 4.51 respectively; $p = 0.783$). ARWMC was not associated with clinical symptoms in iNPH patients, whereas ARWMC was associated with cognitive decline in patients with iNPH mimics, even after adjusting for age, gender and presence of parkinsonism (adjusted β : 1.93, 95% CI: [0.54;3.33]).

Conclusions

The presence of WMC is similar between iNPH and iNPH mimics. WMC was not associated with clinical deficits in patients with iNPH, but with cognitive decline in iNPH mimics. These findings suggest that vascular lesions do not contribute to the symptoms of iNPH. However, WMC play a role in the cognitive deficits presented by patients with iNPH mimics.

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P42**Incidence of anticoagulation and platelet inhibitor therapy in patients operated for subacute – chronic subdural hematomas**

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Introduction

Chronic subdural hematomas (cSDH) are a frequent neurosurgical disease occurring often after a minor head injury, but also following repeated falls, especially in patients under medication with platelet inhibitors and anticoagulation. The symptoms progress slowly and may include altered mental state with cognitive decrease, headaches, focal and transient neurological deficits, rarely seizures, with a possible rather quick „subacute“ deterioration after weeks due to hematoma progression (following a minor head injury or a fall). The risk is increased in multimorbid patients under platelet inhibitor and anticoagulation therapy prescribed for cardio-vascular or cerebro-vascular diseases. This study reviews how many patients operated for chronic, or subacute in chronic subdural hematomas were taking a coagulation decreasing medication.

Material and Methods

Between January 2013 and April 2016, there were 87 patients, 67 men, 20 women, aged between 39-92 years (1923 – 1974) mean age 74,6 years, who required hematoma evacuation with burr holes in 77 cases, (bilateral in 20 persons), craniotomy in 10 (2 patients had a craniotomy plus a burr hole on the opposite side: bilateral cases).

Results

Platelet inhibitors were taken in 30 cases (26 under Aspirin 100mg, 4 under Clopidogrel 75mg). 7 patients were taking NOACS as Xarelto (Rivaroxaban) 10 mg and 20mg. 20 were fully anticoagulated with Marcoumar (3 mg of Phenprocoumon). Therefore a majority i.e., 57 out of 87 patients (65,5%) had blood thinning therapy before neurosurgical treatment.

Discussion

Patients taken blood thinning therapy seem to be at higher risk to develop a subdural hematoma after a fall or minor head injury: This association was found in 57 out of 87 patients, i.e., in 65.5%! The dilemma remains concerning the need for maintaining or re-introducing platelet inhibitors or anticoagulation after surgery for subdural hematomas. The interdisciplinary evaluation of the re-bleeding risk versus vascular re-occlusion or embolism risk should be recommended.

Conclusion

From a neurosurgical point of view the indication for coagulation decreasing drugs should be more strict, especially in multimorbid elderly patients, with a history of repeated falls, as these drugs are frequently associated to subacute and chronic subdural hematomas. This was the case in 65.5% (57 out of 87 patients operated for chronic subdural hematomas).

P43**Simultaneous intracranial – scalp EEG reveal concordant directed connectivity in epileptic spikes**

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Purpose

The identification of pathological networks related to the occurrence of interictal spikes could help to better understand focal epilepsy and to better plan surgery. We aimed to investigate whether directed functional connectivity of interictal spikes seen at both scalp and intracranial EEG revealed the same sources and connectivity pattern using simultaneous intracranial and high-density EEG recordings.

Methods

Intracranial (iEEG) and scalp EEG (256 electrodes) were recorded simultaneously during rest. For iEEG, depth electrodes were implanted in the right orbito-frontal (FOD), amygdala (AD), anterior hippocampus (HAD), posterior hippocampus (HPD), temporal pole (TPD) and posterior temporal gyrus (TPSD). We here present the results of 1 patient (drug-resistant right Temporal Lobe Epilepsy). Fifteen scalp interictal spikes were identified in the right lateral temporal cortex and epochs containing 300 ms before and after the spike were extracted. The corresponding iEEG epochs were then extracted. In the latter, the spike corresponded to the lateral temporal electrodes HPD5-8 (electrode 1 is the deepest and 8 the most superficial) and also seen at HAD5-8. From the scalp EEG, we estimated the cortical source activity, using an individual head model and a distributed linear inverse solution. Only the solution points closest to each intracranial electrode were selected for further analyses. Granger-causal modeling was separately applied to the source and iEEG activity to estimate directed functional connectivity between all solution points/intracranial electrodes. The summed outflow across time and region-to-region connectivity at the spike peak were investigated.

Results

The SP with the strongest source activity was in the right lateral temporal cortex (HPD6), which was the same depicted by iEEG. For the iEEG, the highest summed outflow (driving) was from the right lateral temporal cortex, which was concordant with the strongest summed outflow from the EEG sources. The strongest region-to-region connections for both iEEG and SPs were between lateral temporal contacts.

Conclusions

Source activity, summed outflow and region-to-region connections were concordant between both modalities. This shows the potential of source localization and connectivity analysis to non-invasively determine the epileptogenic zone and study epileptic networks. We are currently analysing a larger cohort of patients.

P44**Increased slow and high frequency oscillations in human hippocampal ECoG during viewing of dynamical landscapes**

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Objective

While the processing of dynamic landscapes and fearful faces elicits an increased hemodynamic response in the mesial temporal lobe, the electrophysiological correlates are still debated.

Methods

Seven epilepsy patients with electrodes implanted in the mesial temporal lobe were visually stimulated with dynamic sequences of neutral landscapes, interleaved with sequences of fearful faces. There were 7 sequences of 24 seconds each. We analyzed the spectral power in landscape and face conditions, detected high frequency oscillations (HFO, 80-500Hz), and quantified cross-frequency coupling between the theta (3-8 Hz) phase and HFO occurrence.

Results

In hippocampal recordings, theta band power was higher in the landscape condition than in the face condition in 4/7 patients ($P < 0.05$). There were more HFO in the landscape condition in all patients ($P < 0.05$). The coupling between theta phase and HFO occurrence was highest at theta phase $\phi = 0$ for the landscapes and lower during the face condition.

Conclusions

The salient theta rhythm and HFOs were associated with dynamic sequences of landscapes and were reduced during the presentation of faces, which may be related to virtual spatial navigation processes in the hippocampus during landscape viewing.

P45**Development of an accurate and cost-effective facial palsy assessment and results of the first data collection for practicality and interrater reliability**

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Background

Facial palsy is the most common cranial nerve lesion (DGN, 2012). Patients with facial palsy have not only restricted movement in the face but also suffer emotional and communicative disorders (Dobel et al., 2013, Van Swearingen et al., 1999). The assessment of the severity of facial palsy has a high prognostic value and significance (Coulson, 2005). To test the functionality of the facial nerve numerous evaluation indices have been developed. In addition, a universal scale is tried to be established for about 45 years (Fattah et al. 2014).

Objective

The main objective of this study was the development of an accurate and cost-effective measurement method for the diagnostic assessment of facial palsy, which already documents minimal movements. The other aim of this study was to test the newly developed practicality scale for measuring facial palsy. Furthermore data on interrater reliability was collected. N = 33.

Method

The facial palsy-assessment has been developed in the context of a master thesis. It implies the diagnosis of the face in frontal view in active movements using a coordinate system, reference lines and landmarks (Figure 1). The intact half of the face is manually holding in the perioral area. The illusion of active movements is avoided by skin shifts (Wolf, 1998). Associated movements contralateral will be reduced (Türk et al., 2012). To test the practicality and interrater reliability 33 probands assessed a patient with facial palsy based on photographs using the new facial palsy-assessment (Figure 2). The results of the findings points to the symmetry were recorded at rest and active movements by questionnaire. With the Likert scale (1932) and open questions the assessment was evaluated. The previous approach of raters and information about the profession were acquired. Subsequently, the review of the issues by means of descriptive statistics and the Fleiss Kappa R significance test was held.

Results

82 % of the reviews were positive implying a high level of acceptance of the facial palsy assessment. The facial palsy assessment showed good practicality with respect to time with a mean of 14.33 ± 6.90 minutes. The orientation on the basis of landmarks scored the highest approval with 82 %. The lowest resonance reached the manually holding in perioral area avoiding the illusion of active movements by skin shifts with a total of 57 % (Table 1). With an interrater reliability of 0.21 the Fleiss Kappa R significance test showed a fair agreement. The p-value indicates a significant level of agreement (< 0.001) between the raters (Table 2).

Conclusion

The present facial palsy-assessment has a good practicality at low costs. The sufficient interrater reliability shows the necessity of continuation of the assessment development.

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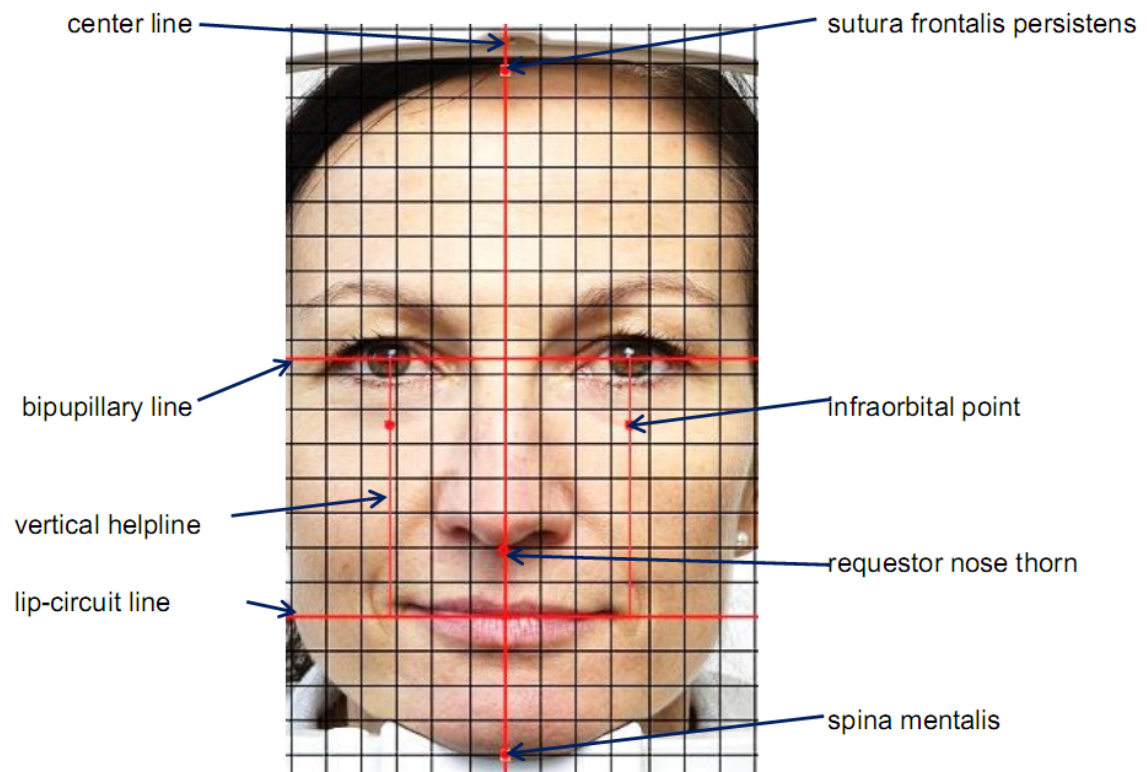


Figure 1. Figure with coordinate system, reference lines and landmarks

Facial Palsy Assessment

		0	1	2	3	4
Resting Symmetrie	Head	Position of the head in relation to the body line				
	Forehead	fold drawing				
	Eye	hanging eyelid				
		everted eyelid				
	Mouth	fold drawing nasolabial				
		depression of the mouth angle				
Active Movements	Forehead	raising eyebrows (wrinkle forehead)				
		pulling down eyebrows				
	Eye	complete lid closure				
		Incomplete lid closure, __ mm				
	Mouth	Retrusion, smiling with closed lips				
		Grin with open mouth				
		Protrusion, speak of a vowel, „O“				
		Speak of a bilabial letter „B“				
	Platysma					

Resting	
Points:	4 = normal symmetry
	3 = mild symmetry
	2 = moderate symmetry
	1 = severe asymmetry
	0 = total asymmetry

Active Movements	
Points:	4 = normal function
	3 = mild dysfunction
	2 = moderate dysfunction
	1 = severe dysfunction
	0 = total paralysis (no movement)

Further Assessment Criteria:

Characteristics	yes	no
Lacrimation		
Hyperacusis		
Gustation impaired		
Problems when eating		
Problems when drinking		
Bite marks (tongue, cheek area)		
Leaking of saliva		
Hemifazial spasm		
Contractures		
Synkinesis		

Figure 2. Facial Palsy Assessment

Table 1. Graphic diagram of the evaluation for the landmarks, reference lines, coordinate system and manually holding in perioral area

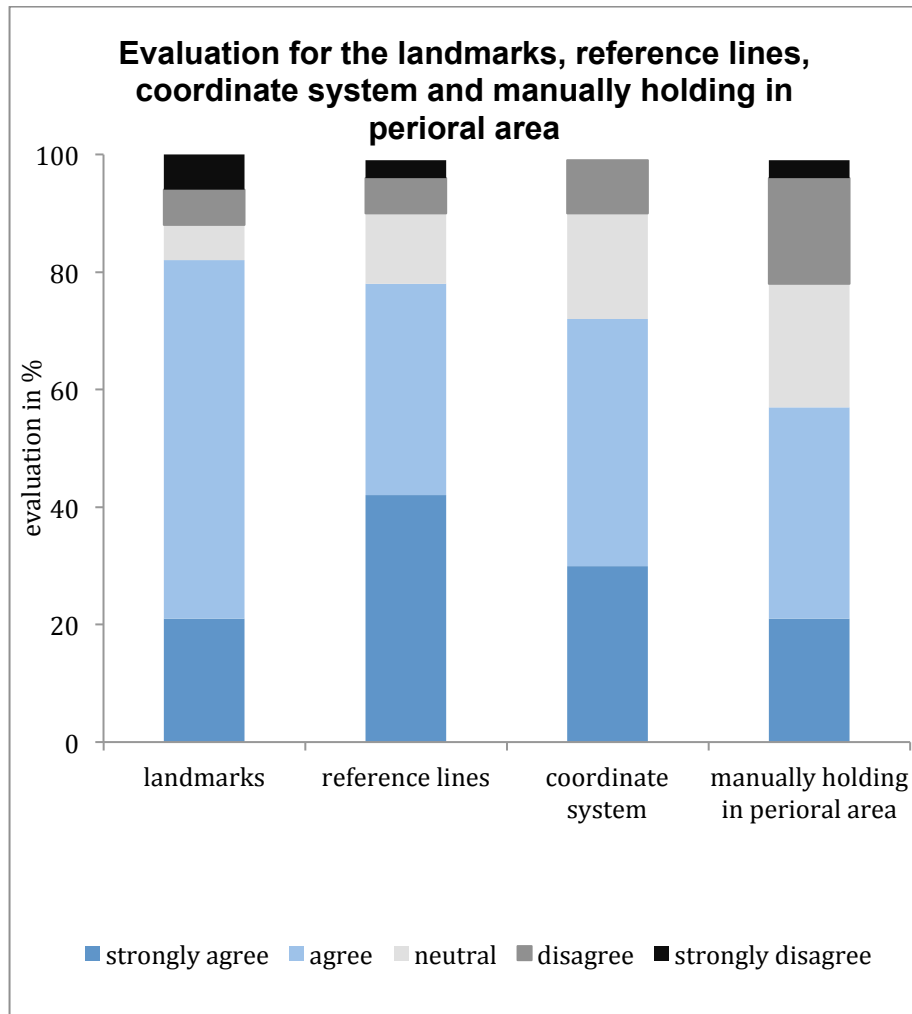
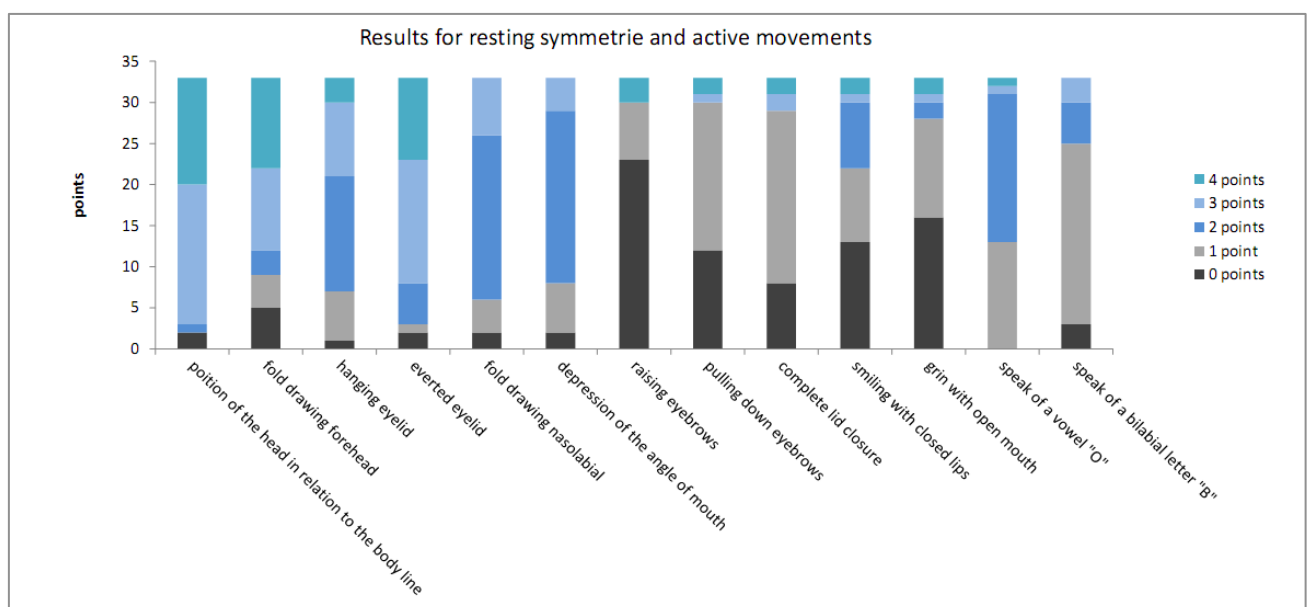


Table 2. Graphic diagram of the results for resting symmetrie and active movements



P46**Diagnostic patterns of sleep- and vigilance tests in distinct causes of excessive daytime sleepiness A retrospective analysis in the Bern sleep database**

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Objective

Sleep and vigilance tests are used in the clinical work-up in order to differentiate between narcolepsy without cataplexy (N), idiopathic hypersomnia (IH), non-organic hypersomnia (NOH), and fatigue syndromes (FS). The aim of this retrospective study was to compare the results of vigilance and sleep tests obtained in a large number of patients with excessive daytime sleepiness (EDS) of various origins with a particular focus on N, IH, NOH and FS.

Methods

From the clinical Bern sleep database (1995-2015) containing 17'822 vigilance and sleep tests (8034 PSGs, 1767 MSLTs, 1340 MWTs, 2057 Steer Clear, 1591 PVTs, 3033 actigraphies), we analysed those NC (97), N (49), IH (60), NOH (126) and FS (143) patients who underwent at least the MSLT and one additional test.

Results

The MWT latencies differentiated better between narcolepsy and idiopathic hypersomnia compared to the MSLT latency ($p < 0.001$ vs $p = 0.083$). As expected MSLT and MWT results were similar in NC and N. We also found no statistical difference for the MSLT and MWT between IH and NOH, underlining the overlap between these disorders. Both reaction time tests (steer clear and PVT) and the inactivity index from actigraphy did not statistically differentiate NOH from organic causes of EDS.

Conclusion

Single vigilance and sleepiness tests have a rather poor differentiating power to separate essential hypersomnias and NOH and approaches combining multiple tests are needed.

P47**Mesio-temporal theta oscillations in a human anxiety task**

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Theta oscillations in mesiotemporal structures including the hippocampus and amygdala have been proposed as a neural signature of anxiety models in rodents, which typically rely on conflicts between approach and avoidance. Recent work has capitalised on magnetoencephalography (MEG) to show that human hippocampal theta oscillations during approach/avoidance conflict relate to learned threat probabilities. Here, we extend these findings by recording local field potentials directly from subcortical structures in humans, using intracranial electroencephalography (iEEG). We recorded iEEG from three patients with mesiotemporal epilepsy during pre-surgical monitoring. Patients completed a "scoop-and-run" computer game emulating operant conflict. They collected monetary tokens under threat of virtual predation. Probability of threat had to be learned by experience while monetary loss was explicitly indicated to participants. At trial start, the player was presented with the predator colour and the possible loss. After a random interval, a monetary token appeared to create behavioural conflict. Power spectra for theta oscillations (1-8 Hz) were extracted using welch transform over 1 s windows and were statistically evaluated at the single-patient level, using independent sample t-tests. Correction for multiple comparisons was performed by non-parametric cluster-based permutations. All three patients showed a significant increase in the power of theta oscillations during 1 s period following the token appearance, compared to a baseline period ($p < 0.05$). Two out of three patients had an additional increase in theta power during 1 s period following the trial start. Only one of the three patients was able to learn the threat probabilities and also showed higher theta power for higher threat level at token appearance. Strikingly, in different contacts, we also observed higher theta power for higher potential loss in the same patient both at trial start and token appearance. The latter effect was partly replicated in the other two patients. In summary, our findings confirm that approach-avoidance conflict increases mesiotemporal theta power in humans. They extend previous MEG results, by suggesting that mesiotemporal theta oscillations relate to expected loss, whether it is explicitly signalled or successfully learned.

P48**Disease pattern of posterior semicircular canal hypofunction on video-head-impulse testing**

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Background

The video-head-impulse test (vHIT) provides a functional assessment of individual semicircular canals (SCC) by quantifying the vestibulo-ocular reflex. With vHIT, isolated posterior SCC hypofunction can occasionally be diagnosed, though this is poorly characterized. Here we retrospectively studied cases with SCC hypofunction restricted to the posterior canals regarding underlying causes and asked how well vHIT-findings correlated with results from calorics and vestibular-evoked myogenic potentials (VEMPs).

Methods

We identified 44 patients (out of 2710 vHIT-datasets) with SCC hypofunction restricted to one/both posterior canals who also received calorics and VEMPs. Pure-tone audiograms were available in 34 cases. We determined gains and cumulative saccade amplitudes and calculated the fraction of cases with isolated posterior SCC involvement vs. those with a more extensive pattern.

Results

Most frequent diagnoses were history of vestibular neuropathy (13/44), vertigo/dizziness of unclear origin (13/44) and Menière's disease (8/44). Seemingly isolated posterior SCC hypofunction on vHIT was accompanied by a deficient horizontal SCC (calorics), saccule and/or utricle ipsilesionally in 33/44 (75%). Ipsilesional hearing-loss was noted in 23/34 (67.6%). The rate of involvement of other parts of the vestibular organ varied, being highest for schwannoma and history of vestibular neuropathy.

Conclusions

Our observations suggest that up to three quarters of patients with isolated posterior SCC hypofunction on vHIT actually have deficits of other parts of the vestibular organ as well. Patients with posterior SCC hypofunction on vHIT should therefore receive additional vestibular testing (i.e., caloric irrigation and VEMPs) to allow a more complete assessment of peripheral vestibular function.

P49**Correlation of Visuospatial Ability and EEG Slowing in Patients with Parkinson's Disease (PD)**

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Background

Visuospatial dysfunction is among the first cognitive symptom in PD and is often predictive for PD-dementia. Furthermore, cognitive status in PD -patients correlates with quantitative EEG. The objective of this cross-sectional study is to investigate the correlation between EEG slowing and visuospatial ability in non-demented PD-patients.

Methods

Fifty-seven non-demented PD-patients (17females/ 40males) were evaluated with a comprehensive neuropsychological test battery and a high-resolution 256-channel EEG was recorded. Visual spatial ability was evaluated using 3 different tests: Clock Drawing Test, Rey-Osterrieth Complex Figure Test (ROCF), and Block Design. A general linear model (GLM) with confounding factors was used for the analysis of correlation between visual-spatial ability and alpha/theta ratio (ATR) in 5 different cortical areas (frontal, central, temporal, parietal and occipital).

Results

A significantly higher ATR for females was found. After correction for this gender difference, the GLM analysis showed no significant correlations between ATR and visual spatial test scores. Therefore, a median split was performed for each cognitive test dividing the patients sample into either a higher or lower performance group. Subsequently, for the lower performance, GLM analysis showed a significant positive correlation between ROCF score and parietal ATR ($b = .59$, $p = .012$) and occipital ATR ($b = .50$, $p = .030$). No significant correlation was found between ATR and the other tests.

Conclusion

Impairment in visuospatial capacity and its correlation with the ATR can be a marker for parietal and occipital dysfunction in PD-patients.

P50**Influence of Age on Quantitative EEG Spectral Markers in Parkinson's Disease (PD)**

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Background and Aims

Age and male gender are known risk factors of PD. A decrease in EEG Alpha/Theta-ratio (ATR) is associated with cognitive decline in PD. The aim of this study is to investigate the influence of demographic parameters (age, education, and gender) with the ATR in patients with PD to identify potential risk factors of PD.

Methods

256-channel EEGs were recorded in 49 non-demented PD patients and 37 healthy controls (HC), matched for age, gender, and education. Relative spectral powers of the EEG for Theta (4-8 Hz), Alpha (8-13 Hz), frequency ranges were calculated. Subsequently, ATR was calculated and averaged for 10 cerebral regions as well as for the complete brain. Wilcoxon test was used to compare PD patients and HC. Furthermore, general linear regression models (GLM) were applied to determine the correlation between demographic and clinical parameters, and ATR.

Results

ATR was significantly decreased in PD patients in all cerebral regions (all $p < 0.05$). This difference was most pronounced in the temporal regions. GLM analyses indicated that these differences were independent of the demographic parameters. ATR was independent of the demographic parameters and therefore could serve as a predictor for PD.

Conclusions

Quantitative EEG measures such as ATR may be used as a marker in the diagnosis of cognitive decline in PD because it is independent of age, education, and gender.

P51**EEG Connectivity in Parkinson's Disease (PD) Patients with and without Mild Cognitive Impairment (MCI)**

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[1] University Hospital Basel, Basel, Switzerland

Background and Objective

Cognitive impairment in several disorders such as Alzheimer's diseases, Dementia with Lewy bodies, and Parkinson's diseases (PD) is associated with changes in EEG connectivity. These changes could be used for the prediction of cognitive decline. The aim of this study was to identify differences in EEG connectivity between PD patients with normal cognition (NC) and mild cognitive impairment (MCI).

Methods

256-channel EEG recordings were obtained from 62 PD patients (mean age: 68 ± 6 y, male/female: 43/23). Diagnosis of PD-MCI was made according to Movement Disorders Society Task Force Guidelines. Connectivity between 76 cortical regions was analysed using the phase lag index (PLI) for different frequency ranges (Delta, Theta, Alpha, and Beta). First, a generalized linear model (GLM) was used to assess connectivity differences between NC and PD-MCI patients. Second, logistic regression was applied to identify which cerebral regions and frequency bands would best distinguish NC from MCI patients.

Results

EEG connectivity differed significantly between NC and PD-MCI patients ($p < 0.01$). With respect to the frequency bands, Theta showed 36 and Beta 6 significantly different connectivities. Compared to NC, PD-MCI patients showed lower PLI values in the Theta frequency band, and higher PLI values in the Beta frequency band. These differences were most frequently seen in connectivities originating in frontal or temporal regions.

Conclusions

EEG connectivity in PD-MCI patients is characterised by increased Beta connectivity and decreased Theta connectivity. Therefore, these findings provide a basis for further EEG connectivity analyses in PD patients.

P52**Andersen-Tawil syndrome (ATS): Novel de novo mutation in the KCNJ2 gene – a case report**

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Introduction

Andersen-Tawil syndrome (ATS) is a rare, multisystem potassium channelopathy with an estimated prevalence less than 1:100 000. The causal mutation is located in the KCNJ2 gene on chromosome 17 which encodes the potassium channel Kir2.1. ATS is characterized by periodic paralysis, cardiac manifestations and different dysmorphic features and may vary even within families. Patients and

Methods

We studied five patients belonging to one family. They all underwent detailed neurological examination and a long exercise nerve conduction test (in accordance with the protocol by McManis). Regarding the dysmorphic features photographic documentation was obtained with the patient's consent. The member with genetically confirmed ATS underwent also cardiac examinations.

Case report of index patient

This 19-year-old man had a three-year history of periodic paralysis in the upper and lower limbs occurring either spontaneously or following exercise. He recovered completely from these attacks and was asymptomatic in between. There was no family history of sudden cardiac death or periodic paralysis. Neurologic examination revealed a short posture and brachydactyly. The potassium levels were normal. The long exercise test showed a progressively decreasing amplitude by >50 % of the compound muscle action potential (cMAP). Finally genetic testing revealed a KCNJ2 mutation with a new substitution of a nucleotide on position 437G>T. Family members Neither the 50-year old mother nor the 58-year old father, nor the 22-year old sister, nor the 21-year old brother had a history of periodic paralysis or cardiac symptoms. Beside the 21-year old brother who presented with a history of gait difficulties, a short posture and dysmorphic features, all other family members showed no abnormalities in the neurological examination. All tested family members had a normal long exercise nerve conduction test and a normal genetic result.

Discussion

The first gene related to ATS was KCNJ2 and could be found in about 60% of patients. Though ATS is inherited by autosomal dominance with variable penetrance, de novo mutations are described in about 30% of cases. We report about a patient with a novel mutation. The position of the KCNJ2 mutation revealed a new substitution of a nucleotide at position 437G>T, which has not been described in the literature yet.

P53**Altered EEG state during induced hypoglycemia in type 1 diabetes**

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Introduction

Hypoglycemia is potentially life-threatening, and regular blood glucose monitoring is inevitable in diabetes therapy. Several studies have reported an association of hypoglycemic state to measurable EEG changes, such as increased spectral power in the low frequency range, and decreased coherence and complexity. However, topographical EEG alterations, indicating changes of brain network dynamics, have never been investigated in hypoglycemia. The aim of this work is to capture topographical field potential changes (EEG microstates) during an insulin-induced hypoglycemia experiment in 17 type-1 diabetic (T1D) patients.

Method

17 volunteers with T1D (8 males, mean age, 55 ± 2.4 years, diabetes duration 28.5 ± 2.6 years, mean HbA1C $8.0 \pm 0.2\%$) underwent induced hypoglycemia, monitored by continuous EEG and repeated blood glucose (BG) samples. A channel-wise time-frequency analysis and a microstates analysis was performed, in broadband [1-40] Hz EEG, in theta band [4.8-7] Hz filtered data, and in alpha band [9-12] Hz filtered data, comparing 5 minutes of both conditions, euglycemia (EU) and hypoglycemia (HYPO).

Results

During HYPO, time-frequency analysis showed a strong power increase for the theta band in mid-parietal regions. Microstate analysis revealed 5 microstates in the broadband, as well as in the alpha and theta band data, with an increase of temporal parameters during HYPO for one specific microstate.

Conclusions

Changes of temporal dynamics of only one specific microstate were found during HYPO compared to EU in all three bandwidths. This indicates that the well-known theta-power increase is specific to the dysfunctioning of one large-scale brain network, of which spatial characteristics still remain to be elucidated by means of high-density EEG and electrical source imaging.

P54**Quantitative EEG (QEEG) in Parkinson's Disease (PD) Patients with and without MCI – Application of the Least Absolute Shrinkage and Selection Operator (LASSO)**

M Chaturvedi [1], B Auschra [1], G Bogaarts [1], U Gschwandtner [1], F Hatz [1], V Roth [2], P Fuhr [1]

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[2] University of Basel, Basel, Switzerland

Background and Aims

QEEG parameters have been shown to be associated with dementia in Parkinson's disease (PD). Studies have shown that these parameters could be useful for prognosis and prediction of dementia in PD. Our aim is to investigate the differences in QEEG measures between samples of PD patients with and without mild cognitive impairment (MCI), and healthy individuals.

Methods

High-resolution 256-channel EEG recordings were obtained in 48 PD patients (MCI/Non-MCI 21/27; age 68.8y [55-84y]; female/male 15/33) and 41 healthy controls (age 70.0y [53-83y]; female/male 20/21). For each participant, relative power for Delta, Theta, Alpha, and Beta frequencies across ten regions of the brain were calculated, as well as median and peak frequencies and the Alpha/Theta-ratio. To identify the most discriminative QEEG parameters, logistic regression using LASSO was applied.

Results

Using the LASSO method, 6 QEEG parameters were included in the regression model. Theta power in the temporal left region and the Alpha/Theta-ratio in the central left region were identified to have the most pronounced effect in differentiating healthy individuals from PD patients. For PD patients 5 QEEG parameters were included, of which Theta and Alpha power in the occipital region were the most discriminative parameters between MCI and non-MCI.

Conclusion

LASSO was successful to identify a small subset of QEEG parameters that optimally distinguish between the subgroups of PD patients. Therefore, the LASSO is a useful scanning tool to identify key discriminative parameters.

P55**Extended EEG in the management of non-convulsive status epilepticus: benefit over routine EEG?**

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Introduction

Continuous EEG monitoring is increasingly used in critically ill patients. We aimed to investigate the benefit of repeated extended in the outcome of people with non-convulsive status epilepticus (SE.)

Methods

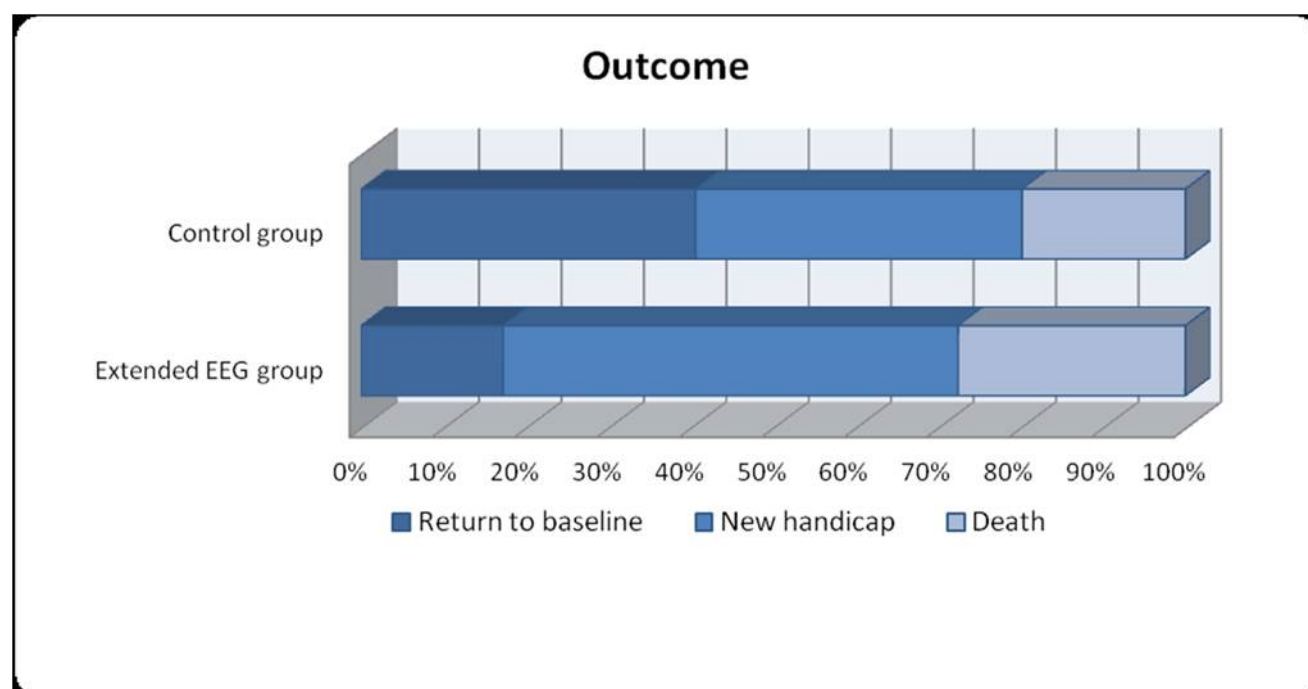
We retrospectively collected a group of 29 consecutive patients with non-convulsive SE admitted in our hospital, which underwent a repeated extended EEG between 2013 and 2015. We compared these patients with a group of 58 patients with non-convulsive SE between 2011 and 2013 managed only routine EEG for the follow-up. The two groups were matched by age. We excluded patients treated with therapeutic coma for treatment of SE. Outcome was categorized as return to baseline, new handicap at hospital discharge and death.

Results

The median age of the two groups was 77 years. Severity of SE was similar in the two groups with similar proportion of potential fatal etiologies (58% in the extended EEG group vs 60%, $p=0.529$) and similar STESS score (median was 3 in both groups $p=0.714$). Acute hospital stay duration showed no significant difference in the extended EEG group ($p=1.31$). When compared, the group of extended EEG group received slightly more antiepileptic drugs (median was 3 in both groups, $p=0.026$). Distribution of the outcome categories at hospital discharge was similar in the two groups ($p=0.129$).

Conclusion

Extended EEG is a useful tool for management of non-convulsive status epilepticus, however does not seem to improve outcome. Benefit of continuous EEG monitoring in non-convulsive SE should be accessed through a randomized trial.



P56**Alteration of global EEG-synchronization in the waking state after sleep deprivation in patients with suspicion of first epileptic seizure**

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Objectives

In patients suspected of epilepsy in which the standard EEG lacks epileptiform abnormalities, EEG after sleep deprivation (SD-EEG) is widely used to improve the diagnostic yield of interictal EEG recordings. The mechanism for the increased presence of epileptiform changes after sleep deprivation is still not totally understood. In this context, our study investigates the differences in global synchronization in the waking state between EEG and SD-EEG in patients suspected of epilepsy.

Methods

14 sequential patients who underwent an EEG and a SD-EEG due to suspicion of first epileptic seizure of loss of consciousness of unknown aetiology were included. We compared the global synchronization in wake stage in both recordings (assessed with a multivariate measure based on the eigenvector distribution of the cross-correlation matrix).

Results

Preliminary data show a decrease in global synchronization in SD-EEG compared to standard EEG without sleep deprivation

Conclusion

Desynchronisation could be the mechanism whereby sleep-deprivation promotes epileptic seizures. Our results are in line with previous studies using various methods to assess the effect of sleep deprivation in synchronization in healthy volunteers.

P57**Relation of automatically detected High Frequency Oscillations (HFOs) with the SOZ and clinical outcome**

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Rationale

While HFOs are gaining acceptance as biomarkers of the epileptogenic zone, their standardized detection is still debated.

Methods

Preoperative invasive recordings were collected during sleep in 17 epilepsy patients, 7 of which had mesial temporal lobe epilepsy (TLE) and 10 extratemporal lobe epilepsy (ETLE). Recordings were analyzed with two automatic detectors, incorporating information from both time and frequency domains. Both detectors have previously been validated independently on two different visually marked datasets. Analyses were conducted separately for ripple (80-250Hz) and fast ripple (FR, 250-500Hz) frequency ranges. Areas with the highest HFO rates were related to the seizure onset zone (SOZ) and to clinical outcome.

Results

With respect to the SOZ, FRs, occurring together with ripples, (FRandRip) were more specific than ripples and FRs separately and correctly identified the SOZ in 12 from 13 patients with good outcome (ILAE1-3). In 4 patients with poor outcome (ILAE 4-6), FRandRips were present also in non-resected non-SOZ areas. Rates of ripples, FRs and FRandRips were higher inside the SOZ than outside. Ripples were more sparsely distributed, and we observed possibly physiological ripples outside the SOZ.

Conclusion

The time-frequency based automatic ripple and FR detection provides a rapid assessment of the potential contribution of HFOs. FRandRips were more specific than ripples and FRs separately in identification of the epileptogenic tissue. The clinical relevance of HFOs was evaluated with fully automatic detectors, which standardize the definition of an HFO. HFOs may prove useful for tailoring the resection area.

P58**Non-invasive detection of fast ripples in low-noise EEG recordings**

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Rationale

Ripples (80-250 Hz) and fast ripples (FRs, 250-500 Hz) are characterized by poor signal-to-noise ratio (SNR), which reduces their visibility in non-invasive recordings. While ripples could be observed in scalp EEG, FR detection has been restricted only to invasive recordings. We report here FR detection in the scalp EEG of epilepsy patients, recorded with low-noise technology.

Methods

One hour scalp EEG was recorded in two patients with focal epilepsy exhibiting interictal spikes and one non-epileptic patient. We used a custom-made low-noise 8-channel amplifier, with noise level $2.3 \text{ nV}/\sqrt{\text{Hz}}$. Electrodes were placed on both hemispheres with impedances below $2 \text{ k}\Omega$. Segments of artifact-free bipolar traces, filtered in the FR band, were selected for analysis. FR rates were obtained semi automatically by combining entropy based amplitude threshold computation and single event visual validation.

Results

For patient 1 (spikes on left side), FR rates averaged across channels were 0.495/min on the left and 0.046/min the right side. For patient 2 (spikes predominantly on the right side), rates were 1.365/min on the left and 1.262/min the right side. For patient 3 (absence of spikes), rates were 0.057/min. The mean FR peak-to-peak amplitude was $3.23 \pm 2.79 \text{ }\mu\text{V}$. The amplitude threshold was $0.51 \pm 0.08 \text{ }\mu\text{V}$ across all channels.

Discussion

FRs in scalp EEG could be detected using optimized low-noise technology. FRs were more frequent in the more epileptogenic regions and may therefore represent epileptic activity. The opportunity to access FRs non-invasively represents a critical step towards the non-invasive investigation of fast neural dynamics.

P59**Biodegradable Magnesium Stent Treatment of Saccular Aneurysms in a Rat Model – Introduction of the Surgical Technique**

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Purpose

There has been a steady increase in the armamentarium of applicable techniques for endovascular occlusion of intracranial aneurysms. However, the role of biodegradable stents has not been evaluated in cerebrovascular research. Experimental animal models are needed for the study of arterial aneurysm biology and its interaction to different embolization materials. The aim of the presented study is to design a safe, fast and standardized surgical technique for basic research of saccular aneurysm treatment with biodegradable stents.

Methods

Saccular aneurysms were created microsurgically by end-to-side anastomosis of an arterial graft from the descending thoracic aorta of a syngeneic rat to the infrarenal abdominal aorta of a Male Wistar rat weighing >500g. Following aneurysm anastomosis, aneurysm embolization was performed by balloon expandable magnesium stent deployment (2,5mm x 6mm, Biotronik, Switzerland) over the aneurysm orifice. The stent system was retrograde introduced from the lower abdominal artery using a modified Seldinger technique.

Results

A total of 42 rats were operated. The mean surgery time, mean anastomosis time and mean suturing time of the artery puncture side were 170±25min, 28±6min and 11±5min respectively. The mortality rate was 7% (n=3). The morbidity rate was 9.5% (n=4), in all 4 cases an in stent thrombosis was found (n=2 early, n=2 late in stent thrombosis).

Conclusion

The results demonstrate the feasibility of a standardized magnesium stent occlusion of saccular sidewall aneurysms in rats with low morbidity and mortality rates. This stent embolization procedure combines the possibility to study novel concepts of bioabsorbable endovascular devices and its molecular aspects in aneurysm healing biology.

P60**Age-related differences in pain intensity, subjective and objective functional impairment and health-related quality of life in lumbar degenerative disc disease**

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Background Context

Demographic changes will lead to an increase of elderly people in our population and consecutively to a higher prevalence of patients suffering from degenerative disc disease (DDD).

Purpose

The goal of this study was to investigate age-related differences in pain intensity, subjective and objective functional impairment and health-related quality of life (HRQoL) in lumbar DDD.

Study Design/Setting

This was a prospective cohort study.

Patient Sample

Adult patients undergoing lumbar spine surgery. Study groups were built according to age < or ≥ 65 years.

Outcome Measures

Patient-reported outcomes instruments (Back and leg pain intensity (Visual analogue scale (VAS)), functional impairment (Oswestry Disability Index (ODI), Roland-Morris Disability Index (RMDI)) and HRQoL (EuroQol-5D (EQ-5D), Short-Form (SF12)) and objective functional impairment (OFI) estimated with the timed up and go (TUG) test) were considered.

Results

A total of 375 patients (162 females, 43.2%) with a mean age of 58.9 years (standard deviation (SD) 15.7) were included, scheduled for lumbar microdiscectomy (n=189, 50.4%), decompression (n=135, 36.0%) or surgical fusion (n=51, 13.6%). There were no differences in subjective pain, functional impairment or HRQoL in patients scheduled for microdiscectomy or decompression. Patients < 65 years scheduled for surgical fusion, however, reported more VAS back pain (5.78 vs. 4.06, p=0.037), more functional impairment (RMDI 12.8 vs. 8.2, p=0.002; ODI 50.8 vs. 40.8, p=0.037) and less HRQoL (EQ-5D 0.437 vs. 0.624, p=0.005; SF-12 MCS 52.9 vs. 42.0, p=0.002). Patients < 65 years scheduled for microdiscectomy (139.9 vs. 123.0, p=0.011) and surgical fusion (125.5 vs. 105.5, p=0.002) had higher TUG T-scores. In univariate analysis, patients < 65 years were 2.9 times as likely as patients ≥ 65 to show OFI (OR 0.34, 95% CI 0.22-0.54, p<0.001). Once this analysis was corrected for baseline group differences, the relationship was insignificant (OR 0.55, 95% CI 0.30-1.02, p=0.056).

Conclusions

Elderly patients scheduled for surgical fusion show less pain, functional impairment and higher HRQoL in subjective and objective measures. In patients scheduled for microdiscectomy and decompression, age has little or no effect on these grading scales.

P61**Validation of the baseline severity stratification of objective functional impairment in lumbar degenerative disc disease**

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Objective

The Timed Up and Go (TUG) test is a simple, objective and standardized measure for objective functional impairment (OFI) in patients with lumbar degenerative disc disease (DDD). The objective of the current work was to validate the OFI baseline severity stratification (BSS).

Methods

Data was collected in a prospective IRB-approved two-center study. Patients were assessed with a panel of pain (Visual analogue scale (VAS) for back and leg pain), functional impairment (Roland-Morris- (RMDI) and Oswestry Disability Index (ODI)) and health-related quality of life (hrQoL; Euro-Qol (EQ-5D), Short Form (SF)-12) measures. OFI BSS was determined using age- and sex-adjusted cut-off values.

Results

N=375 consecutive patients scheduled for lumbar spine surgery were included. Each 1-step increase on the OFI BSS corresponded to an increase of VAS back pain of 0.53, VAS leg pain of 0.69, 1.81 and 5.93 points on the RMDI and ODI, as well as to a decrease of hrQoL of -0.073 on the EQ-5D, -1.99 on the SF-12 physical component summary (PCS) and -1.62 on the SF-12 mental component summary (MCS; all $p < 0.001$). Patients with mild, moderate and severe OFI had increased leg pain by 0.90 ($p = 0.044$), 1.54 and 1.94 ($p < 0.001$), increased ODI by 7.99 ($p = 0.004$), 12.64 and 17.13 ($p < 0.001$) and decreased SF-12 PCS by -2.57 ($p = 0.049$), -3.63 ($p = 0.003$) and -6.23 ($p < 0.001$), respectively.

Conclusion

The most notable finding of this study was an arguably strong relationship between the key subjective measures of function in patients with low back pain, namely the RMDI and ODI. For every 1-step increase in OFI category, the RMDI and ODI saw an increase of 1.81, and 5.93 points on their scales, respectively. When stratified for OFI BSS, patients with mild, moderate and severe OFI saw an increase on the RMDI scale by 3.30, 4.01 and 5.10 points, and on the ODI by 7.99, 12.64 and 17.13 points, compared to patients without OFI. This implies that the clinician can be confident using the OFI BSS presented here to accurately measure function in patients with DDD. The OFI BSS is a valid measure of functional impairment for use in daily clinical practice. The presence of OFI indicates the presence of significant functional impairment on subjective outcome measures.

P62**Burr-Hole Drainage for Chronic Subdural Hematoma under Low-Dose Acetylsalicylic Acid: a Comparative Risk Analysis Study**

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Object

Chronic subdural hematoma (cSDH) is one of the most common neurosurgical diseases typically affecting elderly people. Many of these patients present with coronary artery disease (CAD) and receive antiplatelet therapy, usually Acetylsalicylic acid (ASA). Despite growing clinical relevance, there is still a lack of data focusing on the perioperative management of such patients. The aim of this study is to compare the peri- and postoperative bleeding and cardiovascular complication rates of patients undergoing burr-hole drainage for cSDH with and without discontinuation of low-dose ASA.

Methods

Out of 963 consecutive patients undergoing burr-hole drainage for cSDH 198 (20.5%) patients were under low-dose ASA treatment. In 26 cases (13.1%) ASA was not discontinued (ASA group; ASA discontinuation $\leq$ 7 days preoperatively), while in the rest of the cases (n=172, 86.9%) ASA was discontinued at least for 7 days (control group). The primary outcome measure was recurrent cSDH that required revision surgery owing to clinical symptoms, while secondary outcome measures were postoperative cardiovascular and thromboembolic events, other complications, operation and hospitalization time, morbidity, and mortality.

Results

No statistically significant difference was observed between the two groups regarding recurrence of cSDH (p=1). Cardiovascular event rates, surgical morbidity, and mortality did not significantly differ between patients with and without discontinuation of low-dose-ASA.

Conclusion

Given the lack of guidelines regarding perioperative management with antiplatelet therapy, our findings elucidate one issue, showing comparable recurrence rates with and without discontinuation of ASA in patients undergoing bur-hole drainage for cSDH.

P63**Smartphone navigated insertion of external ventricular drainages**

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Objective

Anatomical landmarks determine primarily the trajectory for placements of external ventricular drainages (EVDs). Nevertheless, non-assisted implantations are frequently complicated by multiple attempts and suboptimal EVDs locations especially if anatomical variants and narrowing of the ventricles exist. Therefore, the authors evaluated the feasibility and accuracy of smartphone-guided angle-adjusted EVDs implantations in both a human artificial and cadaveric model.

Methods

A total of 20 EVDs (skull phantom 8/20, cadaver head 12/20) were implanted. After multi-planar CT 3D reformation a trajectory was set from Kocher's point to the centre of the ipsilateral ventricular frontal horn according to the horizontal and vertical diameter. Intended insertion angles and distances to the catheter tip were measured. The smartphone was calibrated to the mid-cranial sagittal line with the skull in neutral supine position. EVDs were placed using both the measured catheter lengths and smartphone-adjusted insertion angles. Insertion angles and intracranial distance to the catheter tip were measured on postinterventional CT.

Results

All EVDs were placed in the frontal horn of the ipsilateral ventricle as intended. EVDs tip locations showed a mean deviation of 2.76° from the planned trajectory with a 1.93° standard deviation (SD). The mean distance of the EVDs tips to the intended targets was 0.4 cm (SD ± 0.26 cm). The mean duration of measurement of implantation angles and intraventricular lengths was 3 min, and of sterile packing with calibration of the smartphone, drilling and angle-adjusted EVDs implantation 9 min, respectively.

Conclusions

For the first time, a smartphone was used as a tool for placement of EVDs. Our ex vivo study suggests that smartphone-guided EVDs placement represents a precise and fast assisted free-hand technique with a simple and broadly available device.

P64**The severity of a neurosurgical complication correlates with outcome**

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Background

To improve treatment quality, perioperative complications have to be identified and their effects have to be quantified.

Methods

Our department entertains a patient registry, where preoperative state and postoperative outcome are recorded prospectively using neurological and sociological scales. Any deviation from the normal postoperative course is labelled as a complication. Complications are graded by their severity in a therapy-oriented complication score system (Clavien-Dindo-Grading system, CDG). Results are presented at the monthly clinical staff meeting.

Results

Since August 2014 until December 2015, we have registered 325 complications on 1341 patient discharge forms (24%). In 64% of these complications, no or only pharmacological treatment was required. There was a clear correlation of the severity of the complication and the Karnofsky Performance Status (KPS) at discharge ($\rho = -0.3$, $p < 0.001$). The linear fit gave a slope of -6 KPS percentage points per increment of CDG.

Conclusions

A registry of complications must include a severity rating of the complication. The CDG, which was validated for general surgery, is also meaningful in neurosurgery.

P65**Epidemiology and Recurrence Rates of Intracranial Meningioma: Results of a Single Center Cohort Study in Switzerland**

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Object

Meningiomas represent the most common intracranial extraaxial neoplasia in adults, accounting a third of all diagnosed primary tumors of the brain. Incidence increases with age, while females are predominantly affected. Frequently, meningiomas are detected incidentally, showing no symptoms and no significant growth. On the other hand, they might have a huge impact on morbidity. Despite decades of research, relatively little evidence on etiology and epidemiology of meningiomas exists. Aim of our study was to undertake an epidemiological analysis on patients who underwent meningioma surgery over an 8 years time period at our institution in Switzerland.

Methods

We reviewed 187 consecutive patients undergoing meningioma resection between 2008 and 2015 at our institution. Demographic data, medical history, tumor location and side, surgical resection grade (Simpson grade), histo-pathological data, and radiological data was collected and assessed for all patients. Risk factors for recurrence were assessed using univariate and multivariate logistic regression analysis.

Results

Out of 187 consecutive patients undergoing meningioma resection over a period of 8 years (2008-2015) 131 (70.1%) were women ($p < .001$). In 72.2% of the cases, patients were between the age of 45 and 80 years, while more than 40% were in their 6th or 7th decade of life. Meningiomas were classified WHO grade I, II and III in 66.8%, 31.0% and 2.1%, respectively ($p < .001$). MIB-1 proliferation rate was <1 in 7.5%, 1-5 in 52.9%, 6-10 in 22.4%, >10 in 11.8% ($p < .001$). In 82.4% of the cases a Simpson grade 1 and 2 resection was achieved ($p < .001$). Recurrence occurred in 23 patients (12.3%), while higher Simpson grade, WHO grade, and MIB-1 proliferation rate were significant risk factors for recurrence in univariate analysis. After logistic regression analysis only high WHO grade remained a statistical significant risk factor for recurrence (OR 4.72, $p = .022$).

Conclusion

We present recent demographic and epidemiological data of intracranial meningiomas for a single center cohort in Switzerland. Recurrence rate seems to be strongly influenced by WHO grade and less by Simpson resection grade and MIB-1 proliferation rate.

P66**Influence of body mass index on subjective and objective measures of pain, functional impairment and health-related quality of life in lumbar degenerative disc disease**

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Study design

Prospective IRB-approved two-center study. Objective: To analyze the influence of body mass index (BMI) on subjective and objective measures of pain, functional impairment and health-related quality of life (hrQoL).

Background data

Obesity is increasingly encountered in patients with lumbar degenerative disc disease (DDD).

Methods

Comprehensive assessment including the visual analogue scale (VAS) back and leg pain, Roland-Morris (RMDI) and Oswestry Disability Index (ODI), Euro-Qol and short form-12 at baseline and six weeks postoperative. T-scores of objective functional impairment (OFI) were determined using the timed up and go (TUG) test. Pearson's product-moment correlation was run between BMI and all measures at baseline.

Results

A total of n=375 patients with a median BMI of 26.6 kg/m² were included. Of these, n=94 (25.1%) were obese (BMI ≥ 30 kg/m²). Obese patients presented more VAS back pain (mean 4.7 versus (vs.) 3.6, p=0.001) and greater disability on the RMDI (mean 12.6 vs. 11.3, p=0.045). The prevalence and severity of OFI adjusted for age- and sex was similar in obese and non-obese patients. There was a weak to moderate positive correlation between BMI and VAS back pain ($r(373)=0.1552$, p=0.0026), and a weak positive correlation between BMI and both RMDI ($r(373)=0.1138$, p=0.0276) and ODI ($r(373)=0.1075$, p=0.0374). There was no correlation between BMI and TUG T-scores ($r(373)=0.0475$, p=0.3585). Obese patients were as likely as non-obese patients to show a positive six-week response to surgery on the TUG metric (OR 1.31, 95% CI 0.55- 3.11, p=0.543), as well as on all subjective metrics.

Conclusions

Higher VAS back pain, RMDI and ODI correlate with higher BMI in patients with lumbar DDD. Standardized TUG T-scores reflect the patient's degree of OFI well and irrespective of BMI. The TUG test thus is a good candidate for an unbiased objective patient evaluation in patient populations with high prevalence of obesity.

P67**Assessment of the Minimum Clinically Important Difference in the Timed Up and Go (TUG) Test after Surgery for Lumbar Degenerative Disc Disease**

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Background

The timed up and go test (TUG) has previously been described as a reliable tool to evaluate objective functional impairment (OFI) in patients with degenerative disc disease (DDD). The aim of this study was to assess the minimum clinically important difference (MCID) of the TUG test.

Methods

The TUG test (measured in seconds (s)) was correlated to validated patient-reported outcome measures (PROs) of pain intensity (Visual Analogue Scale (VAS) for back and leg pain), functional impairment (Oswestry-Disability-Index (ODI), Roland-Morris-Disability-Index (RMDI)) and health-related quality of life (HRQoL) measures (Short Form-12 (SF12) and EuroQol 5D (EQ5D)). Three established methods were used to establish anchor-based MCID values using responders of the following PROs (VAS back and leg pain, ODI, RMDI, EQ5D index and SF12 PCS) as anchor: 1) average change, 2) minimum detectable change (MDC) and 3) change difference approach.

Results

One hundred patients with a mean age of 56.2 years (SD 16.1), n=57 (57%) males, n=45 undergoing microdiscectomy, n=35 lumbar decompression and n=20 fusion surgery were studied. The three MCID computation methods revealed a range of MCID values according to the used PRO from 0.9 s (ODI based on the change difference approach) to 6.0s (EQ5D index based on the MDC approach) with a mean MCID of 3.4 s for all measured PROs.

Conclusions

The MCID for the TUG test time is highly variable depending on the computation technique used. The average TUG MCID was 3.4 s using all three methods and all anchors.

P68**The Influence of Lunar Phases and Zodiac Sign 'Leo' on Perioperative Complications and Outcome in Elective Spine Surgery**

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Objective

To assess the influence of 'unfavorable' lunar or zodiac constellations on perioperative complications and outcome in elective surgery for degenerative disc disease (DDD).

Methods

Retrospective database analysis including n=924 patients. Using uni- and multivariate logistic regression, the likelihood for intraoperative complications, re-do surgeries, as well as the clinical outcome at 4-weeks was analyzed for surgeries performed during waxing moon, full moon, and dates when the moon passed through the zodiac sign 'Leo'.

Results

In multivariate analysis, patients operated on during waxing moon were 1.54 times as likely as patients who were operated on during waning moon to suffer from an intraoperative complication (OR 1.54, 95%CI 1.07-2.21, p=0.019). In contrast, there was a trend towards fewer re-do surgeries for surgery during waxing moon (OR 0.51, 95%CI 0.23-1.16, p=0.109) while the 4-week responder status was similar (OR 0.73, 95%CI 0.47-1.14, p=0.169). Full moon and zodiac sign 'Leo' did not increase the likelihood for complications, re-do surgeries or unfavorable outcomes.

Conclusions

We found no influence of 'unfavorable' lunar or zodiac constellations on the 4-week responder status or the revision rate that would justify a moon-calendar based selection approach to elective spine surgery dates. However, the fact that patients undergoing surgery during waxing moon were more likely to suffer from an intraoperative complication is a surprising curiosity and defies our ability to find a rational explanation.

P69**Transdural arterial recruitment to brain AVM. Clinical and management implications. A prospective cohort series.**

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Background

The occurrence of transdural arterial recruitment (TDAR) in association with brain arteriovenous malformation (bAVM) is uncommon and the reason for TDAR is not understood. The aim of this cohort study is to examine patient and bAVM characteristics associated with TDAR and the implication of TDAR on management.

Methods

A prospective surgical database of bAVM was examined. Cases previously treated elsewhere or incompletely examined by digital subtraction angiographic assessment were excluded. Three studies on this cohort were performed, characteristics associated with TDAR, the relationship between TDAR and neurological deficits unassociated with hemorrhage (NDUH) and the impact upon outcome from surgery of TDAR. Regression models were performed.

Results

Of 769 patients with complete digital subtraction angiography (DSA) that had no previous treatment, 51 (6.6%) were found to have TDAR. The presence of TDAR was associated with increasing age ($p < 0.01$; OR: 1.05; 95%CI: 1.02 to 1.07), presentation with NDUH ($p < 0.01$; OR: 2.71; 95%CI: 1.29 to 5.71), increasing size ($p < 0.01$; OR 1.57; 95%CI: 1.29 to 1.91) and combined supply from both anterior and posterior circulations ($p = 0.02$; OR 2.37; 95%CI: 1.17 to 4.78). Further analysis of TDAR cases comparing those with and without NDUH found an association of larger size [6.6 cm (2.9 SD) compared with 4.7 cm (1.8SD); $p < 0.01$] and combined supply from both anterior and posterior circulations (relative risk: 2.5; 95% CI: 1.0-6.2; $p = 0.04$) to be associated with a NDUH presentation. For the 632 patients undergoing surgery, there was an increased risk of complications of surgery (where this produced a new permanent neurological deficit at 12 months of a mRS >1) with: size; location in eloquent brain; deep venous drainage; increasing age; and the absence of presentation with hemorrhage. TDAR was not associated with an increased risk of complications of surgery.

Conclusion

TDAR occurs in older aged patients with larger bAVM. TDAR are also more likely to be associated with bAVM presenting with NDUH. The likely explanation for the presence of TDAR is a secondary recruitment arising as a consequence of shear stress rather than a primary vascular supply present from the earliest development of the bAVM.

P70**Combined endovascular and microsurgical intervention in the treatment of arteriovenous malformations – a hybrid approach**

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Aims

Despite recent advances in endovascular technology, surgical techniques and stereotactic radiosurgery the effective treatment of brain arteriovenous malformation (AVM) remains a challenge. Prevention of haemorrhage is achieved by either single or multimodal treatments. In the presented study we summarise our experience in combined endovascular embolization and microsurgical removal of brain AVM using a hybrid operating room.

Methods

We retrospectively reviewed all cases of AVMs treated in our department between November 2010 and December 2015. We recorded the following characteristics: age, gender, Spetzler-Martin and Buffalo grades, clinical symptoms at presentation and discharge, pre- and postsurgical treatments, pre-, intra-, and post-operative angiographic findings, duration of surgical and endovascular procedures, complications, obliteration rates and remnants of treated AVMs.

Results

Out of total 49 patients 18 (37%) underwent hybrid surgery. Most patients (15 out of 18, 83%) who underwent hybrid surgery had Spetzler-Martin grade I and II AVMs. In this subgroup patients tended to be young (mean age 41 ± 19 years) and frequently presented with ruptured AVM (13 out of 18, 72%). All cases with eventual hybrid-surgery had intraoperative complete occlusion of their AVM without any remnant, regrowth, or new symptoms (10 ± 9 months post-interventional).

Conclusions

Hybrid treatment is an effective, safe, and efficient treatment option for brain AVMs with low Spetzler-Martin grades in symptomatic patients. Short term clinical and radiological outcome is favourable. We support the use of intraoperative angiography for radical excision of AVMs. In our experience radical removal of brain AVMs was facilitated by a combined endovascular and microsurgical treatment in a hybrid operating room.

P71

Comparative analysis of inflammatory processes during cervical and lumbar degenerative disc disease(DDD)

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Purpose

To investigate the inflammatory processes in the sites of disc degeneration in the lumbar and cervical spine by a cytokine gene array and subsequent qPCR.

Materials and Methods

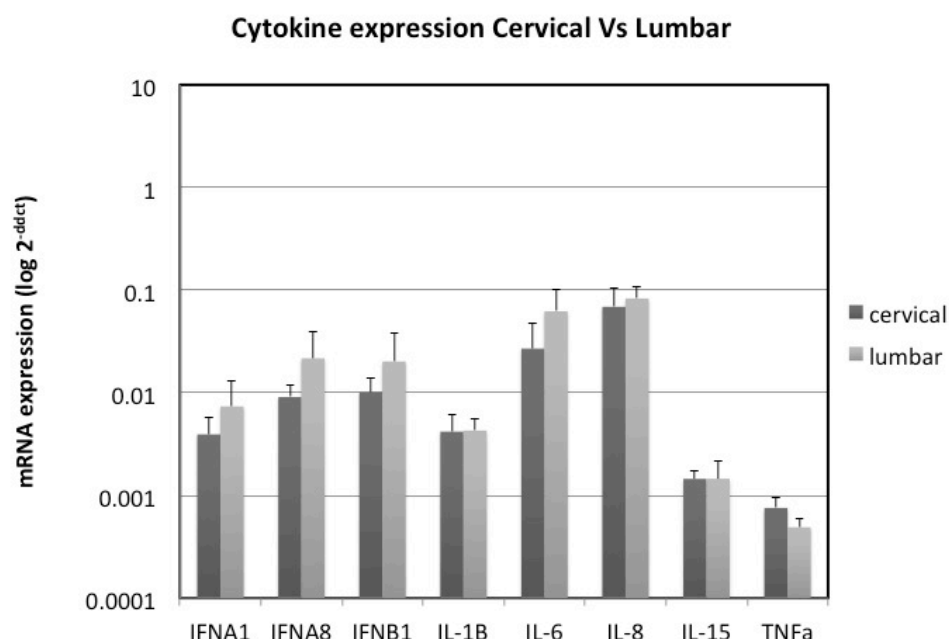
Disc samples were obtained from 31 patients undergoing discectomy, 11 men and 20 women, with a mean age of 56 years. RNA was extracted by Trizol/Chloroform method and examined for 28 cytokines by a gene array (n=6) followed up by standard qPCR for eight selected cytokines on all samples. Samples had the following characteristics: site=24x cervical and 7x lumbar; pathology=11x disc herniation and 20x degenerative disease (all $\geq$ grade 3); level=3x one level discectomy and 18x multilevel discectomy. For the patients that underwent multilevel discectomy, one sample was gathered. The nucleus pulposus (NP) and annulus fibrosus (AF) of the lumbar samples were separately examined. Results were statistically analyzed by two-sample Kolmogorov-Smirnov test with a significance level of $p \leq 0.05$.

Results

In both, cervical and lumbar discs, the interleukines IL-6 and IL-8 were found to be the overall highest expressed genes, whereas the expression of IL-1 β , TNF- α and IL-15 was comparatively low. Three previously unreported cytokines could be detected: the interferones INA1, IFNA8 and IFNB1. No statistically significant difference was found between cervical and lumbar samples, or between AF and NP samples for any of the investigated genes. Also, no correlation was found between gene expression and gender, age or the extent of the operation (single/multilevel).

Conclusions

Our results show that no major differences exist in the inflammatory profile of cervical and lumbar degenerated discs, indicating that novel anti-inflammatory treatments may be applicable independent of the degeneration site. The high expression of IL-6 and IL-8 supports their described relevance in nociception and matrix degradation. Although IL-1 β and TNF- α are well described to play a role in the pathogenesis of DDD, their expression was comparatively low. This study is the first to describe the expression of type I interferons (alpha and beta) during disc degeneration. Although their role in DDD is currently unclear, they are often described to have immunomodulatory effects and may hence be a reactive attempt to inhibit inflammation in the disc. Further studies will be required to identify their disc-specific function as well as the role of IL-15, which has also been sparsely investigated thus far.



P72**Posterior fossa aneurysms: epidemiology, patterns of care and outcomes from the Swiss SOS national registry.**

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Introduction

Posterior circulation (p-fossa) aneurysms presenting with subarachnoid hemorrhage (aSAH) remain a challenge and the treatment is often tailored according to individual experts' experience. We report data from the Swiss SOS national registry to provide epidemiological characterization of affected subjects, treatment pattern and outcomes.

Methods

From January 1st 2009 to December 31st 2015, data from 1941 patients with aSAH were recorded. 167 p-fossa aneurysms accounted for 12.8% of cases. Outcome at discharge and at 1 year was assessed with mRS and then dichotomized into good (mRS ≤ 2) and poor (mRS ≥ 3).

Results

143 patients received treatment for p-fossa aneurysm. Mean age was 57.2 years (range 19.788). 24 patients were neither clipped nor coiled for unclear reasons. PICA (31.7%) and basilar tip (27.5) were the most frequent locations. The most frequent WFNS grade was 5 (33.3%) and the most frequent aSAH grade was Fisher 3 (44.7%). 82.5% of patients were treated by endovascular means and 15.3% with clipping. 15 patients (9%) developed vasospasm requiring endovascular treatment. Hydrocephalus necessitating shunting was correlated with poorer mRS at discharge ($p=0.001$) and at 1 year ($p=0.04$). Patients with DIND were more likely to present with poor mRS at 1 year ($p=0.01$). Patients treated by coiling presented mRS values similar to surgical patients ($p=0.5$) both at discharge and at 1 year.

Conclusions

SAH patients due to p-fossa aneurysms from the Swiss SOS registry presented a favourable outcome in the majority of cases (62.3% mRS ≤ 2). Patients improved after discharge and only WFNS 3-5 patients remained significantly more disabled at 1 year. Despite multicentric data collection over 7 years, the cohort remains too small to perform subgroup analysis. Thus, robust evidence regarding treatment options for ruptured posterior fossa aneurysms is still lacking.

P73**Semi-quantitative assessment of flow dynamics during indocyanine green video-angiography in the treatment of intracranial dural arteriovenous fistulas: technical note.**

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Introduction

Intracranial dural arteriovenous fistulas (iDAVFs) are rare acquired arteriovenous shunts whose treatment of choice is disconnection of venous drainage from arterial supply. Previous reports described the use of Flow800 software during IG video-angiography (IG-VA) to facilitate the identification of arterialized veins and to confirm complete iDAVFs shunt interruption. Here we first report a real-time application of color maps and semi-quantitative flow analysis by Flow800 software.

Methods

iDAVF angioarchitecture is explored with a 5-mg IG intravenous bolus administration and observed using Flow800 software. Flow800 software provides a real-time color-coded map at the level of different regions of interest (ROIs) displayed as fluorescence (transit) curves. The parameters considered for confrontation in different ROIs are: time to peak, (time interval between initial appearance of fluorescence within the field of view and maximum fluorescence intensity); time to half- maximal fluorescence (time between initial appearance of fluorescence within the field of view and 50% of maximum signal). Arterialized veins display an abnormal fluorescence peak occurring before the half maximal fluorescence peak of normal veins. After iDAVF disconnection, the repeated IG-VA and semi-quantitative flow analysis with Flow800 software at the same ROIs shows that the latency to filling of the draining vein reaches the one of the surrounding normal veins.

Discussion

Conventional IG-VA during iDAVF surgery may not be able to recognize the slight time difference of fluorescence peak between arteries, arterialized veins and non-arterialized veins. The reliability of conventional IG-VA may be increased by the implementation of a color map and semi-quantitative analysis of IG transit curves with the Flow 800 software.

Conclusions

Treatment of iDAVF remains challenging and direct identification of the draining vein during surgery is essential to the resolution of the arteriovenous shunt thus preventing iDAVF recurrence. Here we describe the first report of real-time application of semi-quantitative flow analysis by Flow 800 software for more confident identification of iDAVFs draining veins. We believe that semi-quantitative flow analysis by Flow 800 software is a reproducible technique that may overcome the limitations of conventional IG-VA in the treatment of iDAVFs.

P74**Intraoperative neurophysiological markers of the success of STN-DBS: microelectrode recording, stimulation, local field potential?**

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Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is advocated in patients with advanced Parkinson's disease (PD). Microelectrode recording (MER) is one of the targeting modalities performed in conjunction with stimulation. In addition, the occurrence of β oscillations of the local field potentials (LFP) has been suggested as another targeting modality. The goal of this study was to evaluate which intraoperative neurophysiological markers are most predictive of the STN-DBS efficacy. Thirty-nine consecutive patients with PD and with a follow up of to at least one year post surgery were included. The efficacy of STN-DBS was evaluated using the MDS-UPDRS part III (score OFF antiparkinsonian medication and ON DBS at one year, versus preoperative OFF antiparkinsonian medication). Intraoperative stimulation thresholds were determined for the therapeutic effects on rigidity and for the internal capsule stimulation (MER and stimulation: Neurostar, GE; 130Hz, 60 μ s). LFP were recorded from the macrocontact of the microelectrodes (FHC, USA) at the time it was positioned for stimulation (MR plus, GE). β power, computed from LFP [11-31Hz], recorded at the site chosen for stimulation were compared to that recorded above the STN. Coefficients of determination (R^2) were computed to analyze which proportion of the variance of the STN-DBS efficacy could be explained by these neurophysiological markers. None significant linear regression was found between the STN-DBS efficacy and the stimulation thresholds of either the effects on rigidity, the magnitude of rigidity improvement, the threshold of internal capsule stimulation or the stimulation range ($R^2=0.03$, $p=0.34$; $R^2=0.09$; $R^2=0.09$, $p=0.07$; $R^2=0.07$; $p=0.16$; respectively). A light but significant linear correlation was found between the STN-DBS efficacy and the distance over which STN cells were recorded ($R^2=0.20$, $p<0.02$). Sigmoid regressions were found significant between the change in β power and the STN-DBS efficacy ($R^2=0.78$, $p<0.001$). Here intraoperative stimulation thresholds had no predictive value of the STN-DBS success. New directional electrodes, allowing adaptation of the electrical field dedicated to avoid stimulation of the internal capsule, should reduce again the role of intraoperative stimulation. Changes in β power accounted for 80% of the variance of the STN-DBS efficacy, confirming the major interest of this intraoperative neurophysiological marker.

Acknowledgments

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P75**Analyzing complications in Lumbar Spine surgery in regards to treatment costs, length of hospital stay and short-term clinical outcome**

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Objective

To evaluate the Clavien-Dindo classification grade (CDG) of surgical complications in regards to usefulness, reliability and its correlation with treatment costs and duration of hospitalization following surgery in a neurosurgical patient population in a prospective, single-center study.

Methods

138 consecutive patients undergoing lumbar spine surgery at the Department of Neurosurgery, University Hospital of Zürich, Switzerland were included in this prospective single center study. General patient data, type and duration of surgical procedure, duration of hospitalization and costs of treatments were noted and documented through the Departments' patient registry. Furthermore, CDG, Rankin scale, Karnofsky performance status and McCormick grade were scored at the time of admission, discharge and 6 week follow up.

Results

We found a strong correlation of the CDG with cost of treatment, duration of hospitalization as well as a strong negative correlation with outcome at discharge and Karnofsky Performance Status and at 6 weeks follow-up.

Conclusion

The Clavien-Dindo grade is a useful and reliable tool to measure short-term complications in a neurosurgical patient population. Despite its relative "generic" nature it is able to cover complications in a specialized field of surgery such as spinal neurosurgery and correlates strongly with duration of hospitalization, costs and clinical outcome measures.

P76**The Effect of Aspirin on Morbidity in Meningioma Surgery.**

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Object

Meningiomas are considered the most common primary brain tumors in adults, while representing a third of all diagnosed primary neoplasms of the brain. Although many of them are considered histologically benign, they might influence morbidity significantly, especially through high blood loss during surgery. As meningioma incidence risk increases with age, many of the patients present with other comorbidities like coronary artery disease (CAD) and receive antithrombotic therapy, usually Acetylsalicylic acid (ASA). The aim of this study is to compare the peri- and postoperative bleeding and cardiovascular complication rates of patients undergoing meningioma surgery in ASA users and non-users.

Methods

Out of 187 consecutive patients undergoing meningioma resection, 24 (12.8%) patients were under low-dose ASA treatment, while 163 (87.2%) patients were non-users. The primary outcome measure were peri- and postoperative bleeding events, while secondary outcome measures were postoperative cardiovascular and thromboembolic events, operation and hospitalization time, morbidity, and mortality.

Results

No statistically significant difference was observed between the two groups regarding bleeding events ($p=.7$), cardiovascular events, surgical morbidity, and mortality. A sub-analysis evaluating the effect of the postoperative resumption time of ASA on the bleeding rate will be presented.

Conclusion

Our results show comparable bleeding and cardiovascular complication rates in ASA users and non-users implicating that antithrombotic therapy with ASA does not affect morbidity in meningioma surgery.

P77**Elective craniotomy for intraventricular tumors: postoperative challenges**

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Objective

Following craniotomy for intraventricular tumors patients often show a tendency for delayed postoperative awakening. Consequently early postoperative neurological monitoring is challenging and a head CT is frequently ordered to rule out postoperative complications. Our goal was to quantify time to extubation and perioperative complications after elective craniotomies for intraventricular tumors as compared to craniotomies for extraventricular lesions.

Methods

We screened our prospective database of elective craniotomies on patients older than 18 years from November 2011 until June 2015 for intraventricular tumors. Extubation was aimed for postoperatively in the OR for all cases. CT scanning within 48 hours postoperatively was performed only for unexpected neurological findings or prolonged somnolence. The two patient groups (intraventricular vs. extraventricular tumors) were compared in terms of time to extubation, need for emergency head CT and urgent operative revision within 48 hours. The prospective study on elective craniotomies was registered at ClinicalTrials.gov [NCT01987648].

Results

Of 738 elective craniotomies 20 (2.7%) were performed for intraventricular tumors. Mean time to extubation after skin closure for patients with extraventricular lesions (group 1) was 25.9 minutes (± 30.0) and 37.6 minutes (± 29.5) for patients with intraventricular tumors (group 2) ($p = 0.079$). In group 2 urgent head CTs were statistically significantly more often ordered than in group 1 (rate 30% and 8%, respectively, odds ratio 5.17 (95% confidence interval 1.91-13.98), $p = 0.004$). The rate for urgent operative intervention within 48 hours in group 2 was 5% (1 case, external ventricular drain) compared to 1% in group 1 (8 cases, OR 4.67, 95% CI 0.56-39.23, $p = 0.220$).

Conclusion

Craniotomy for intraventricular tumors is associated with a higher rate of critical events postoperatively such as need for head CTs, surgical revision, and a tendency for delayed emergence from anesthesia. This cohort requires especially close and diligent postoperative monitoring.

P78**Effect of Aneurysm Wall Cellularity in Aneurysm healing Following Coil Embolization – Assessment in a Rat Saccular Aneurysm Modell**

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Purpose

Despite significant technical advances the recanalization rates after endovascular therapy remains a clinical challenge. A hallmark of human intracranial aneurysm is wall degeneration and mural cell loss. Vascular smooth muscle cells can undergo phenotypic modulation, proliferate, synthesise collagen matrix and organize luminal thrombus. The aim of our study was to assess the aneurysm healing process following coil embolization in cell rich and decellularized aneurysms.

Methods

Saccular aneurysms were created microsurgically by end-to-side anastomosis of an arterial graft from the descending thoracic aorta of a syngeneic donor rat to the infrarenal abdominal aorta of a recipient Male Wistar rat. Untreated arterial grafts were immediately transplanted, whereas aneurysm with loss of mural cells were decellularized by sodium dodecyl sulfate prior to implantation. Coil implantation was performed with 2cm of 360° 3mm Coils (Stryker) during aneurysm anastomosis. The aneurysms were harvested on day 3, 7 or 21 and underwent macroscopic and histological analysis.

Results

A total of 39 rats were included for macroscopic and histologic analysis. While aneurysms with cell rich walls (n=20) showed a linear course of thrombosis and neointima formation, decellularized aneurysms (n=19) showed marked inflammatory aneurysm wall degradation with significant increased recanalization rates (p=0.021) three weeks following coil embolization. Aneurysm size remained stable in both groups over time and none of the aneurysms ruptured.

Conclusion

Aneurysms with loss of mural cells are prone for wall degeneration, increased inflammation, and aneurysm recanalization following intraluminal coil treatment.

P79**Treatment of ruptured PICA aneurysms in the endovascular era. Evidence from the Swiss SOS national database.**

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Introduction

PICA aneurysms represent a small subgroup of patients who present with an aneurysmal subarachnoid hemorrhage (aSAH). We performed a subgroup analysis of the results following treatment of PICA versus non PICA posterior circulation aneurysms from the Swiss SOS registry.

Methods

Patients' records of 167 treated posterior circulation aSAH were reviewed from January 1st 2009 to December 31st 2015 from the Swiss SOS registry. PICA was the more frequent location (31.7%), followed by basilar tip aneurysms (27.5%). The clinical outcome at discharge and at 1 year were assessed using the modified Rankin score (mRS) dichotomized into good ($mRS \leq 2$) and poor ($mRS \geq 3$). Associations between clinical outcome and following factors were tested: WFNS and Fisher grade at admission, epilepsy, cranial nerve deficit, ventricular hematoma, vasospasm, delayed ischemic neurological deficit (DIND), hydrocephalus and aneurysm dimensions.

Results

The PICA group accounted for 52 treated aneurysms and the non-PICA group for 115 aneurysms. Most posterior circulation aneurysms were treated using endovascular procedures (stent, coiling, combination). Despite a minority of PICA aneurysms were treated by clipping (34%), it remains much more likely than in the other posterior circulation locations (OR 0.24; 95% CI 0.12 to 0.50). No significant difference was demonstrated between both groups regarding presence of cranial nerve deficit, intubated status on admission, cerebrospinal fluid diversion and requirement of dilation angioplasty for vasospasm. There was no statistical difference between the mRS at discharge and at 1 year between the PICA and the non-PICA groups (good mRS was present in 69.2 % at discharge and in 66.6% at 1 year in PICA patients and versus 53.0% at discharge and in 60.3% at 1 year in non-PICA patients). There was no association between treatment modality and outcome for neither groups PICA or non-PICA.

Conclusions

PICA is a prevalent site for posterior circulation aneurysms where treatments remain challenging due to their variable anatomic features and proximity to lower cranial nerves. Both microsurgical and endovascular treatments are valid options for their treatment with similar outcomes. In this series, the outcomes following treatment for PICA aneurysms are good in over 69.2% at discharge and 66.6% after 1 year. In addition, these outcomes are similar to that of non PICA aneurysms in contrast to that described in literature.

P80**Complications and outcome of craniotomies in the sitting position in neurosurgery**

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Objective

Complications of using the sitting position (SP) in neurosurgical procedures have been reported in the literature; however, it is still applied routinely. A current survey in Switzerland is missing. The goal of this retrospective study is to present the current indications, complications and outcomes of patients operated in the SP.

Methods

All patients who underwent craniotomies in the SP from March 2011 until June 2015 at the Neurosurgical Department of the Kantonsspital Aarau, Switzerland were included. All the patients were screened for cardiac shunts. The intraoperative monitoring featured precordial sonography. Further data, e.g. loss of blood, hypotonia, bradycardia, duration of the procedure were recorded. Postoperative complications were assessed.

Results

A total of 94 patients were screened. Forty cases (39 patients) were included in the study. The major reason for exclusion was 'procedures without craniotomy' (e.g. infiltration of the Gasserian ganglion). Patients' characteristics were as follows: mean age 46 years (12-85), female patients 57%, mean BMI 26 kg/m². Seventy-three percent of the patients hosted tumors, 15% vascular pathologies and 12% Chiari I malformations. The mean ASA score was 2. The following approaches were used: suboccipital 88%, transsagittal and retromastoideal 5% each, supracerebellar/infratentorial 2%. The mean duration of surgery was 206 min, the mean blood loss 204 ml. Hypotension, bradycardia and venous air embolism (VAE) were detected in 15%, 52% and 5% of the patients. Postoperative complications, seen in 15% of the patients, included rebleeding (7%), surgical site infection (2%), CSF Fistula (2%), and hydrocephalus (5%). All VAEs were asymptomatic. Duration of intubation was 0-17 days (mean 0.65); tracheotomies were not indicated. No thromboembolic events or tension pneumocephalus occurred. One patient with a severe subarachnoidal hemorrhage died, leading to a mortality rate of 2%. The mean Glasgow outcome score was 4.5 (3-5). Mean Karnofsky on last follow-up in tumor patients was 87% (70-100).

Conclusion

The incidence of specific complications of the SP, such as symptomatic VAE, thromboembolism, or tension pneumocephalus is low. As the incidences of other complications seem to be predominantly related to the localization and the nature of the surgical target, the surgeon and OR team have to be encouraged to use the positioning that best suits their demands.

P81**Intraventricular glioblastoma – A rare localization of a common intracerebral tumor**

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Background

Glioblastoma multiforme (GBM) represents approx. 25% of all intracranial tumors in adults and is the most common primary brain tumor. In two thirds of cases, is the frontotemporal region affected, although this tumor can occur anywhere in the central nervous system. The intraventricular region as primary localization is extremely rare and only 29 cases have been reported, so far. Surgical gross total resection with concomitant radiation and chemotherapy is the standard therapy for best survival.

Methods

We report on six cases of histologically confirmed intraventricular GBM's who underwent biopsy or subtotal tumor resection at our department and were admitted between December 2015 and May 2016.

Results

All six cases with intraventricular mass underwent at least tumor biopsy to confirm the histology of GBM. The mean age was 58.2 ± 15.7 years, the youngest patient was 26 years old. In terms of gender, there were 4 males and 2 females involved. The main clinical manifestations were neuropsychological deficits with personality changes, memory disorders and fatigue. Three patients presented with paresis, and one was symptomatic with headache and diffuse body pain. One patient presented with a fulminant loss of consciousness and was treated on the ICU for several days with an EVD. Four patients underwent biopsy only and two patients underwent craniotomy and subtotal tumor resection. All lesions were localized in the body of the lateral ventricle, in one case in the anterior horn, in another case in the central part of the lateral ventricle and in two cases in the posterior horn and the trigone. In the remaining two cases the tumor was found in the body of the inferior horn. The 2 patients who underwent surgery had the GBM localized in the posterior and the inferior horn and a parietooccipital approach over the trigone was used. Adjuvant radiation and chemotherapy followed in 4 patients.

Conclusion

Glioblastoma multiforme is the most common primary brain tumor, but the intraventricular localization is very rare and has a rather poor prognosis due to the fact, that gross total resection mostly can not be achieved. Surgical removal might be attempted only if subtotal resection can be achieved.

P82**Surgical Occlusion of Spinal Dural Arteriovenous Fistula controlled by Intraoperative Spinal Angiography**

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Background

Spinal dural arteriovenous fistula (SDAVF) is a rare cause of progressive myelopathy in predominantly middle aged men. Treatment modalities include surgical obliteration and endovascular embolization. In surgically treated cases, failure of obliteration is reported in up to five percent. The aim of this technical note is to present a safe procedure with complete SDAVF occlusion, verified by an intraoperative spinal angiography.

Methods

We report on three cases with progressive leg weakness that underwent surgical obliteration of their SDAVF with intraoperative spinal angiography. The spinal dural AV-Fistula of the first patient had the main feeder arising from the right T11 segmental artery, which supplied as well the Artery of Adamkiewicz. The SDAVF of the second patient was initially treated endovascularly, but after 5 months he clinically deteriorated due to recanalization of the SDAVF by a small branch of the T12 segmental artery. The third case was primarily planned for surgical occlusion.

Results

The procedures were done in prone position and the popliteal artery gained the access for the spinal angiography. An angiography was performed pre- and intraoperative after clipping of the fistula point and occlusion of the SDAVF. Access through popliteal artery for spinal angiography showed to be beneficial and safe, allowing the sheath to be left in place during procedure. Therefore, the intraoperative angiography could be available within 15 minutes. The intraoperative angiography showed in one case a misplacement of the clip with failure of fistula occlusion and the clip was directly repositioned. All final intraoperative angiographies showed a complete occlusion of the fistula.

Conclusion

Our presented cases confirm that the intraoperative spinal angiography is a feasible and safe procedure without any additional complications. The intraoperative angiography is important to localize the fistula and to prove successful obliteration.

P83**Microsurgical Aneurysm Treatment under Endovascular Temporary Balloon Occlusion: Technical Note**

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Background

Recurrent aneurysms after clipping/coiling or anatomical demanding localization, endovascular occlusion may not be suitable due to wide neck or risk of parent or perforator vessel occlusion. Moreover, standard clipping could fail due to insufficient proximal control leading to incomplete occlusion or intraoperative rupture. Temporary balloon occlusion (TBO) of the parent vessel might lower the risk of intraoperative rupture and reduce the pressure in the aneurysm sac to facilitate the dissection/clipping. We present our experience and setup of TBO during aneurysm clipping.

Methods

We report on 5 cases of intracranial aneurysms clipped with TBO treated in our department between 2011-2016. The first case was a recurrent aneurysm of the AComA (20x12mm), that underwent clipping 31 years ago. An attempt to coil the reperfused aneurysm 2 y earlier failed. The second patient suffered SAH after rupture of a basilar tip aneurysm (4x15mm), endovascular occlusion was not indicated due to risk of PCA and SCA branch occlusion. The third case was a recurrent MCA bifurcation aneurysm (11x9mm) that underwent prior clipping and coiling. Patient number four presented with an SAH and ICH with a ruptured MCA aneurysm. The fifth case was a ruptured, partially thrombosed basilar aneurysm (11x8x8mm) with secondary wall hematoma without SAH.

Results

All cases underwent combined surgical and endovascular procedure in our hybrid OR. After craniotomy and dissection of the parent vessel and branches needed for visual control and partial aneurysm dissection, the intraluminal balloon was inserted thru the femoral artery and inflated. No complications during balloon inflation or rupture of the aneurysm prior to clipping occurred. The duration of TBO varied between 10 and 20 min. The two BA and the MCA aneurysms could be completely occluded, the recurrent aneurysms of the AComA and the MCA bifurcation showed a small remnant at the neck which was wrapped in one case. All patients except one showed a postoperative good recovery with a GOS 5. A 72 yo patient with a MCA aneurysm with SAH and ICH, initially presenting with a GCS 7/WFNS 4, did not recover from the impaired LOC and died during ICU treatment.

Conclusion

Intraoperative TBO is a safe procedure with no additional morbidity using a standardized protocol. In addition, iDSA within the environment of the hybrid OR offers the evaluation of aneurysm occlusion including 3D reconstructions to exclude aneurysm remnants.

P84**Non - invasive ICP measurement in brain tumors: Can an increase in ICP be objectified?**

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Background

Since decades, neurosurgeons and neurooncologists assumed, that the mass effect of brain tumors with peritumoral edema might lead to increased intracranial pressure (ICP), but no clinical evidence has proven this fact. The aim of this study was to verify the paradigm of intracranial tumors causing intracranial hypertension.

Methods

In the study period from December 2014 until November 2015 a total of 20 patients with brain tumors were included and non-invasive ICP measurement was performed. This technique of non-invasive ICP measurement is based on simultaneous measurement of ophthalmic artery (OA) blood flow in the intracranial and extracranial segments of the OA with two-depth transcranial Doppler. We investigated in a retrospective study the correlation of absolute ICP values with clinical and radiological parameters that define signs of intracranial hypertension in patients with brain tumors.

Results

In this study population 12 patients were male and 8 patients were female. The mean age in our population was 63.8 years (± 13.2). Overall 28 measurements were reliable and repeatable and were included into this analysis. A neurological deficit was observed in 90% of cases. Clinical signs of raised intracranial hypertension were found in 6 patients (30%) presented as headache. The tumor volume was in the range from 7.07 cm³ to 220.27 cm³ and the perilesional edema was in range between zero and 238.26 cm³. All non-invasive ICP measurements were in the normal range of 15 mmHg, with a mean of 9.19 mmHg and a ICP max. of 16.72 mmHg. As the ICP was measured on both sides separately, it is noteworthy that the ICP was generally not increased on the side of the tumor location. In a bivariate association analysis, the only statistically significant correlation with max. ICP ($p=0.02$) and mean ICP ($p=0.01$) was found with neurological deficits. Surprisingly, patients with neurological deficits had a lower ICP than patients without. In a multivariate model (neurological deficits & max. tumor diameter) the neurological deficits were again associated with lower values of max. ICP (95% CI: -9.67, -3.17; $p<0.001$) and max. tumor diameter was associated with larger value of the max. ICP (95% CI: 0.05, 1.17 $p=0.033$).

Conclusion

Brain tumors presenting with classical mass effect such as peritumoral edema, midline shift, and neurological deficits might not lead to raised intracranial pressure. These results need to be confirmed in a larger study population.

P85**Cranioplasty after decompressive craniectomy: risk factors for complications and infection.**

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Background

Decompressive craniectomy due to intracranial hypertension is usually followed by a cranioplasty (CP). In our institution the delay to CP is 3 months. Although CP is a routine procedure, it is associated with significant rates of post-operative complications. The aim of our study was to analyze possible risk factors.

Methods

We retrospectively collected demographic, clinical and radiological data of patients who underwent autologous or heterologous CP in our institution between 01/2007-12/2012 and were followed-up for ≥ 30 days post-operatively. The primary endpoint was presence of any complications associated with cranioplasty; in addition, infectious complications were separately analyzed (secondary endpoint).

Results

We identified 112 patients who underwent CP, of which 93 met the inclusion criteria. The mean delay to CP was 100.6 days (SD 90.5); mean craniectomy size 107.7cm² (SD 39.6). Thirty-nine (41.5%) patients had at least one complication, of which 25 (26.6%) required surgical treatment. Sixteen infections (17.0%) resulted in 11 (11.7%) flap removals. More than two cranial surgeries before CP was a risk factor for overall complications (OR 4.4, CI 1.4-13.9, $p=.007$) and infection (OR 3.7, CI 1.1-12.1, $p=.03$). Time to CP was longer in patients with complications, including infectious (126.9 vs 93.9, $p=.001$). Complication rates did not differ between CP performed before/after 3 months delay post-craniectomy. In univariate analysis larger size of craniectomy ($p<.001$), longer duration of surgery ($p=.02$) and higher number of surgeries before CP ($p=.04$) were predictors of complication. In multivariate analysis only higher number of surgeries before CP remained an independent predictor of complication ($p=.02$).

Conclusions

Despite being a routine procedure cranioplasty carries a high rate of post-surgical complications. Our data suggests that ≥ 2 cranial surgeries before cranioplasty, larger craniectomy size and longer surgery time are risk factors for post-operative complications. More studies are needed to determine the optimal delay to cranioplasty.

P86**Cranioplasty: Is surgical education safe?**

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Background

Patient safety aspects and the residents' role in spine surgery within a structured training program have recently been investigated. The current work deals with residency training safety aspects for cranioplasty (CP), a standard neurosurgical cranial procedure.

Methods

Retrospective two-center study comparing consecutive patients undergoing CP by a supervised neurosurgery resident (teaching cases) with a consecutive series of patients operated on by a board certified faculty neurosurgeon (BCFN; non-teaching cases). The primary endpoint was occurrence of a postoperative complication. Secondary endpoints were severity (Ibanez degree) of postoperative complications, surgical site infections (SSI) requiring CP removal and patients' clinical outcome measured with the modified Rankin Scale (mRS).

Results

A total of n=240 CPs (n=137 (57.1%) teaching and n=103 (42.9%) non-teaching cases) were analyzed. The mean teaching case operation time was longer (129.2 vs. 115.8 min, $p<0.001$), while there was no difference in the estimated blood loss (mean 243.3 vs. 223.1 ml, $p=0.444$). Supervised residents were as likely as BCFNs to have a postoperative complication (OR 0.77, 95% CI 0.42-1.39, $p=0.385$) and the severity was comparable (Pearson χ^2 7.62, $p=0.106$). Teaching cases were as likely as non-teaching cases to experience a SSI requiring CP removal (OR 1.66, 95% CI 0.69-4.04, $p=0.261$). Also, the likelihood for postoperative improvement on the mRS was similar for patients in both groups (OR 1.11, 95% CI 0.62-2.00, $p=0.719$).

Conclusions

A relatively simple cranial procedure, such as CP, can be safely done by a supervised neurosurgery resident without increasing complications or compromising patients' outcomes.

P87**Giant intraosseous meningioma mimicking fibrous dysplasia**

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We illustrate a case of a giant primary intraosseous meningiomas (PIMs) with optic nerve compression treated by partial resection. A 48-year-old female presented with visual disturbances exophthalmus, diplopia and eye pain due to optic nerve compression. The patient had a past history of fibrous dysplasia treated surgically with partial resection by ENT in 2010. Histology confirmed the diagnosis. Two years later she presented with further decrease in visual acuity and diffuse hyperostosis. In this context she underwent a neurosurgical procedure consisting in craniotomy and further partial resection of the lesion including optic canal decompression. The second pathological examination demonstrated an extensive meningioma (WHO grade I) of the skull base. We recommend that in cases of diffuse hyperostosis the differential diagnosis include diffuse intraosseous meningioma. If complete surgical resection is not achievable, a biopsy to confirm the diagnosis is recommended. Treatment options include complete or partial resection followed by adjuvant radiotherapy.

Table 1

Type	Description	Subclassification
I	Purely extracalvarial	Not applicable
II	Purely calvarial	B (skull base) C (convexity)
III	Calvarial with extracalvarial extension	B (skull base) C (convexity)

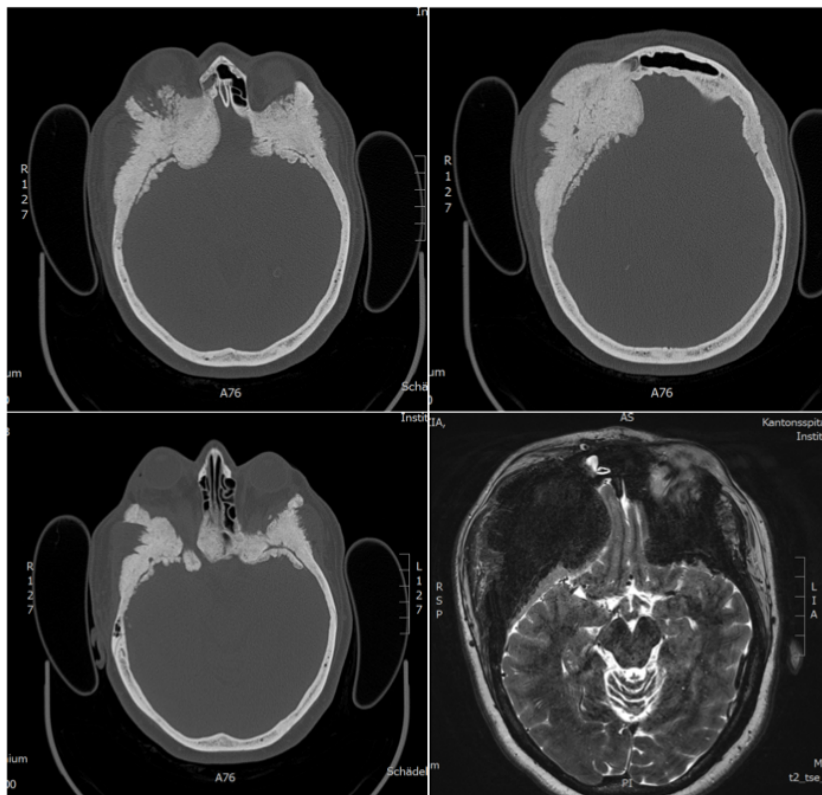


Image 1

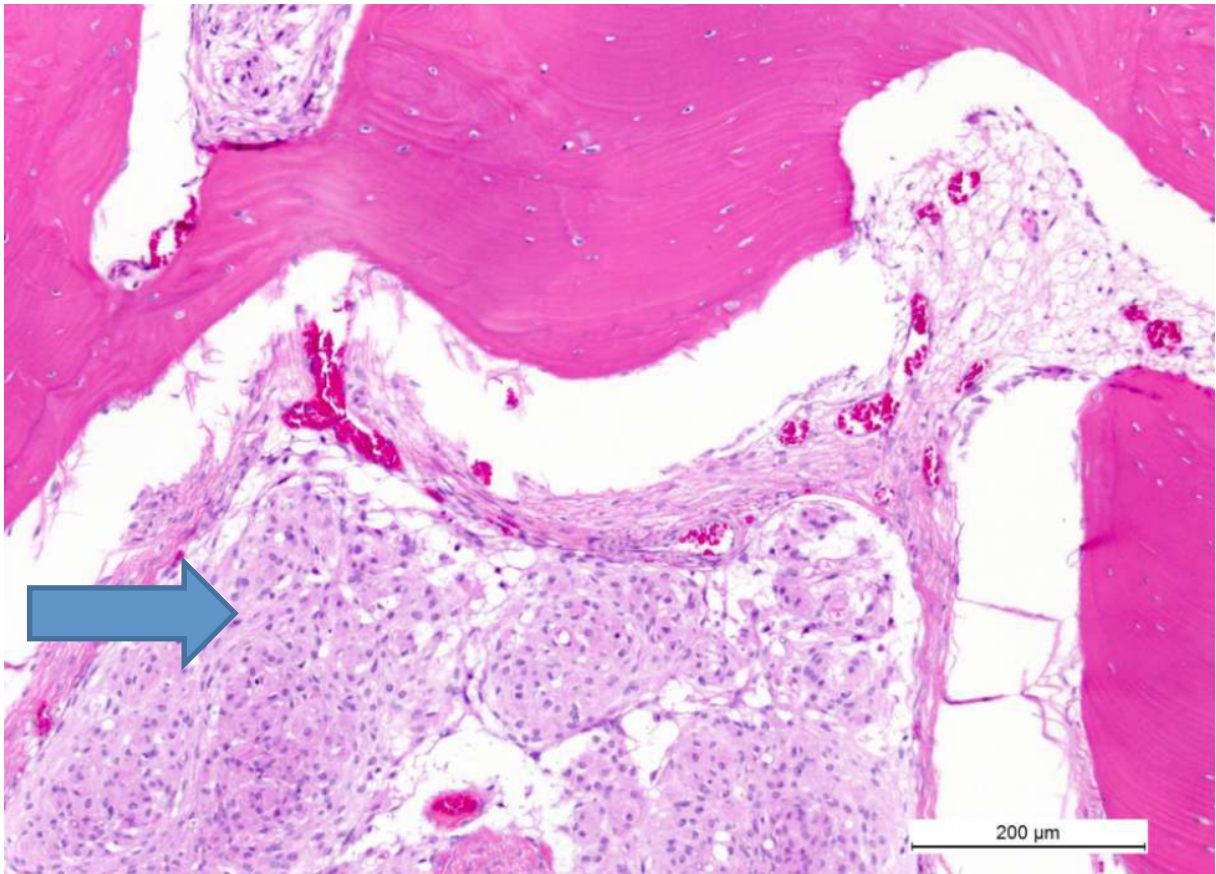


Image 2

P88**Delayed death one week following a gunshot injury due to air embolism**

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Introduction

Gunshot injuries can be fatal or may be survived with neurological and neuropsychological deficits. At KSGR they are rare with one patient every 4-7 years. We report an exceptional case with a survival during one week followed by death due to air embolism.

Case report

This 39 years old man was admitted following a right frontal to left parietal parasagittal gunshot injury after having being found comatose with CGS 4, but still breathing and coughing, with reacting and symmetrical pupils. He was intubated and brought to our hospital. (see Figs. 1-4). After stabilization of the hemodynamic situation, he underwent a neurosurgical wound revision with hemostasis, removal of some epidural blood, some bony fragments and protruding necrotic brain tissue, leaving some epidural blood layer „padding“ the injured parietal midline. The wounds were adapted without achieving a watertight closure. He remained stable and was transferred on day 7 to the medical ward for further care. On day 8 he suddenly died after an attempt to mobilize him, i.e., to put him in an upright position.

Result of the medico-legal examination

Gas accumulation in the right sided heart chambers. Gunshot induced bi-parietal hemorrhagic lesions with 1 cm epidural hematoma extending to the frontal region, torn superior sagittal sinus (see Fig.5) with elevated about 4 cm large fragments of the parietal bone.

Discussion

This patient didn't die during the first days, but after one week, following what is routinely done in head injured patients: a progressive mobilization with verticalization. Autopsy revealed air embolism as cause of death. Some air has probably entered through a not watertight closure of the skin, and the blood left on the dura didn't occlude enough the way to the torn superior sagittal sinus.

Conclusion

The risk of air embolism is well known, but the awareness of this risk is not present in daily routine especially in the very rare case of a gunshot injury to the brain. The upright position is known to be a trigger for air aspiration in patients with open head injuries or operations performed in sitting position because of negative pressure in the superior vena cava and the right atrium. The risk is comparable to the one during removal a central venous catheter, which should be performed in horizontal to Trendelburg position. This knowledge should be implemented into the checklists and guidelines, as recommendations to doctors, physiotherapists and nursing staff.

P89**Gangliocytomas of the sellar region: Is it really a rare entity?**

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Background

Gangliocytoma of the sellar region are considered to be rare lesions. We found in our series of sellar lesions, one case of gangliocytoma coupled with a GH secreting pituitary adenoma. We decided to perform a systematic review of the literature to report the cases described till now and to summarize the recent information from literature on the subject.

Methods

We performed a systematic review through PubMed focusing on articles reporting gangliocytoma of the sellar region. Epidemiological data, clinical presentation, histochemical and radiological features and follow-up data were analyzed.

Results

Fifty-five articles reporting 129 cases of gangliocytoma of the sellar region were analysed. Our case was also included. 85% of cases were associated with pituitary adenomas. Patients were more frequently female and presented with hyperprolactinemia (44%) or visual disturbances (47%) when the sellar gangliocytoma was isolated, or with acromegalic manifestations (67%) when the gangliocytoma was associated with a pituitary adenoma. A higher prevalence of mixed GH-PRL adenomas was found at immunohistochemistry. Gangliocytomas were purely intrasellar in 25% of cases and suprasellar in 30% of cases. A wider extension was found in 40% of cases. The follow-up period was variable among papers and endocrine remission was reported in 81% of cases.

Conclusions

With 130 cases reported in literature, gangliocytomas of the sellar region are not that rare and is at present an emerging clinical entity. The association with pituitary adenomas should always be looked for. Mixed GH PRL adenomas are the most common subtype of adenomas found in association with gangliocytomas. Further studies need to be performed to clarify the pathogenesis and the significance of this association.

P90**Computer assisted virtual planning and surgical template fabrication for fronto-orbital advancement: Evaluation of Advancement using 3D Photographs**

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Introduction

Fronto-orbital advancement (FOA) surgery using computer-assisted design (CAD)/computed-assisted manufacturing (CAM) and 3D surgical templates leads to reconstructions based on standardized measurements, precludes subjective remodeling, and seems to be overall safe and feasible. However, the extent of overcorrection that should be undertaken is still under debate. The aim of this study was to assess the feasibility of 3D photography for the objective evaluation the FOA.

Methods

Twelve patients underwent FOA surgery based on the CAM/CAD technique. Three patients had a uni-lateral and one patient a bi-lateral coronal synostosis and eight patients a metopic synostosis. Virtual surgical planning was performed using SurgiCase® (CMF, v5.0, Materialise, Belgium). The postoperative evaluation is done using 3D photographs of the patients and comparing them to the pre-surgical planning. Landmarks used for the objective evaluation are the supraorbital angle, supraorbital foramen, lateral orbita wall, and the tip of the fronto-orbital bandeau.

Results.

The objective evaluation of the undertaken FOA using 3D photographs is feasible while no postoperative CT scan is needed. Results of the objective postoperative evaluation compared to the pre-surgical planning will be presented.

Conclusions

This novel technique allows us to evaluate in an objective and precise matter the extent of under-correction/relapse after FOA surgery. Accordingly, the additional over-correction that should be undertaken can be better estimated and calculated and thereafter implemented intraoperatively.

P91**Intraoperative neuromonitoring of language during tumor resection under general anesthesia**

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A major issue in tumor resection is to avoid significant deficits for important functions, such as motor or language functions, when their substrate lies beside the resection site. At present, the technique used to monitor language integrity necessitates the conscious participation of the patients through awake neurosurgery (Duffau et al., 2008). However, this technique has many limitations and its use remains constrained. Our team is developing a new technique to monitor language functions under general anesthesia. Our technique relies on the collection of neurophysiological activity of the eloquent language area while the patient, under general anesthesia, receives language stimulation. The language stimulation consists in an oddball task, where identical sequences of syllables are repeated with the insertion of deviant stimuli differing on one phonemic feature (eg., ba-ba-ba-da). This oddball paradigm is classically used for indexing the integrity of phonemic processing. A well-known component, called mismatch negativity (MMN), is generated between 150 to 200 ms after the beginning of the deviant syllable and localized in the superior temporal lobe (Näätänen et al., 2007). The signal is being collected with cortical electrodes when eloquent language areas are exhibited for the needs of the neurosurgery, and with sub-dermal scalp electrodes placed especially in regard to Broca's and Wernicke's areas in the other cases. We have collected preliminary data from 15 patients aged between 29 and 82 years old (mean = 62 years; sd = 15) who underwent tumor resection, 6 in the right and 9 in the left hemisphere. Two important results emerge from these preliminary analyses. First, we were able to demonstrate a significant difference in response to standard vs. deviant stimuli. Second, the detection of this difference may depend upon the bispectral index (BIS). Indeed, it was detected more frequently in patients with BIS values above 50 compared to patients with lower BIS values, without reaching significance in this preliminary group. To our knowledge, this is the first demonstration that some language functions could be measured under general anesthesia. Further work is needed to confirm these preliminary results and to determine how this signal can be exploited throughout the surgery to preserve at most language integrity.

Acknowledgement

We thank the Private Fondation of University Hospital of Geneva for their financial support (Project Research and Development n° 10-2015-I).

P92**Sexual Dysfunction in Patients with Good-Grade Aneurysmal Subarachnoid Hemorrhage**

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Introduction

Although neurological and neurocognitive outcomes have previously been studied after aneurysmal subarachnoid hemorrhage (aSAH), the impact of aSAH on sexual life has not been investigated. Our aim was to assess the consequences of aSAH on sexual experience in patients with otherwise favourable neurological outcome.

Methods

Anonymous standardized questionnaires concerning sexual functioning including the International Index of Erectile Function (IIEF) and Female Sexual Function Index (FSFI) respectively and a subjective statement were completed by 33 aSAH patients treated at the Kantonsspital St. Gallen between 2005 and 2013. All of them had a favourable neurological outcome (Glasgow Outcome Scale (GOS) 4 and 5).

Results

10 patients (31.3%) deplored a subjective deterioration of sexual pleasure after bleeding. Sexual dysfunction according to the FSFI criteria affected 9/19 female patients (47.37%) and all 19 women (100%) had a hypoactive sexual desire disorder (HSDD). Erectile dysfunction was present in 7/14 male patients (50%).

Conclusion

This first evaluation of sexuality after aSAH with otherwise favorable neurological outcome suggests that sexual dysfunction is common in this population. Therefore, sexual health should consistently be addressed in the follow up of these patients.

P93**The value of short-term pain relief in predicting the 1-month outcome of lumbar transforaminal epidural steroid injections**

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Objective

To determine whether short-term leg pain alleviation following computed tomography-guided transforaminal epidural steroid injections can predict the 1-month outcome.

Design

Prospective observational. Setting: Tertiary radiology department. Subjects: n=57 consecutive patients with radiculopathy secondary to a lumbar disc herniation.

Methods

Study components were visual analog scale leg and back pain at baseline, 15, 30, 45 minutes, 1, 2, and 4 hours, on days 1-14, as well as at 1 month. Health-related quality of life and functional impairment were assessed using the short form-12 and Oswestry disability index. Patients who reported >80% persisting leg pain, as well as patients who underwent a second injection or an operation within 1 month were defined as 'non-responders'. Logistic regression was used to analyze the effect size of the relationship between >50% pain relief at any given study visit and responder status.

Results

Patients experiencing a >50% pain reduction 4 hours after the injection were 3.38 times as likely to be responders as those experiencing ≤50% pain reduction (OR 3.38, 95%CI 1.07-10.65). The effect decreased between day 1-2, but re-appeared on day 3 and was strongest on day 6 (OR 6.87, 95%CI 1.99-23.72). It remained significant until day 14.

Conclusions

The results of this study can guide physicians in managing patients with lumbar disc herniations: A <50% leg pain relief within 1 week after a transforaminal epidural steroid injection predicts an unfavorable 1-month outcome and suggests that other treatment options may be considered at an earlier point in time.

P94**Impact of the volumes of different tumor components in glioblastoma on overall survival**

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Aim

The primary aim of the study is to determine the impact of the volumes of different tumor components in glioblastoma (GBM) on the overall survival (OS). Thereby, we try to determine the concept of invasiveness in relation to the tumor volumes.

Methods

A retrospective analysis of 65 patients with GBM operated in our department between 2009 and 2014 was performed. Clinical and demographic data was retained from the tumor database of the University Hospital Basel. Volumetric data was collected from the preoperative magnetic resonance images (MRI) using the visual ABC-Method. For every patient, four different preoperative volumes in ml were calculated: enhancing tumor, non-enhancing tumor, necrosis and edema. On postoperative MRI, enhancing residual volume in ml was measured for every patient as well. Multivariable survival models will be used to associate the different tumor volumes with OS adjusting for the potential confounder age and the postoperative enhancing residual tumor volumes (as a measure of treatment differences).

Results

We analyze the data of 40 (61.5%) male and 25 (38.5%) female patients with a median age at the day of surgery of 62.7 (interquartile range 27-79) years. During follow up 60 patients (92.3%) died, median survival was 398 (interquartile range 24-1745) days. The results of the survival analysis and potential associations of enhancing, non-enhancing and total tumor volume (enhancing + non-enhancing + necrosis) with the overall survival will be presented.

Conclusions

Conclusions will be presented together with the final results.

P95**Early Rupture of Giant Basilar Aneurysm following Leo stenting**

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Abstract Risk of treatment of intracranial aneurysms (IA) associated with complex angioarchitecture located in the posterior circulation is high. Advances in the endovascular armamentarium, such as flow diversion and stent devices finally give such IA a treatment option. Delayed IA rupture following flow diversion is rare but often a fatal complication. Large and giant IA are likely to pose a higher risk due to the large amount of clot formation with its suspected detrimental effect on the IA wall. However, the exact mechanisms leading to delayed rupture are poorly understood. Often used flow diverters associated with this complication include Pipeline, Silk, and Surpass devices. So far, to the best of our knowledge, early rupture after IA treatment using a Leo self-expanding stent (Balt, Montmorency, France) has not been described. We present a case of a 60-year-old patient with a progressively growing giant basilar artery aneurysm (size 3.4x3.2x3cm) who underwent a procedure using a Leo stent applied as a matrix stent to place a flow diverter at a later date. After an uneventful procedure the patient experienced an unexpected fatal subarachnoid hemorrhage on the fourth day post IA occlusion. Autopsy demonstrated extensive subarachnoid hemorrhage, large intraluminal thrombus and a ruptured IA wall. The aneurysm ruptured in a linear manner and was completely filled with a clot that seemed to have outgrown the thin aneurysm wall. The Leo stent was in its intended location and there was no sign of in-stent-thrombosis. Histology showed thinning and degenerative changes of the aneurysm wall accompanied by a sparse neutrophilic and histiocytic (CD68+) inflammatory infiltrate adjacent to the site of rupture, consistent with recently published cases of IA rupture in the literature. We will present detailed histological findings, review previously reported cases, and the described alleged possible mechanisms for early rupture.

P96

Multilevel severe radiculopathy from an extraneural glioblastoma cervical metastasis: A case report and literature review

D Starnoni [1]

[1] CHUV, Lausanne, Switzerland

Background

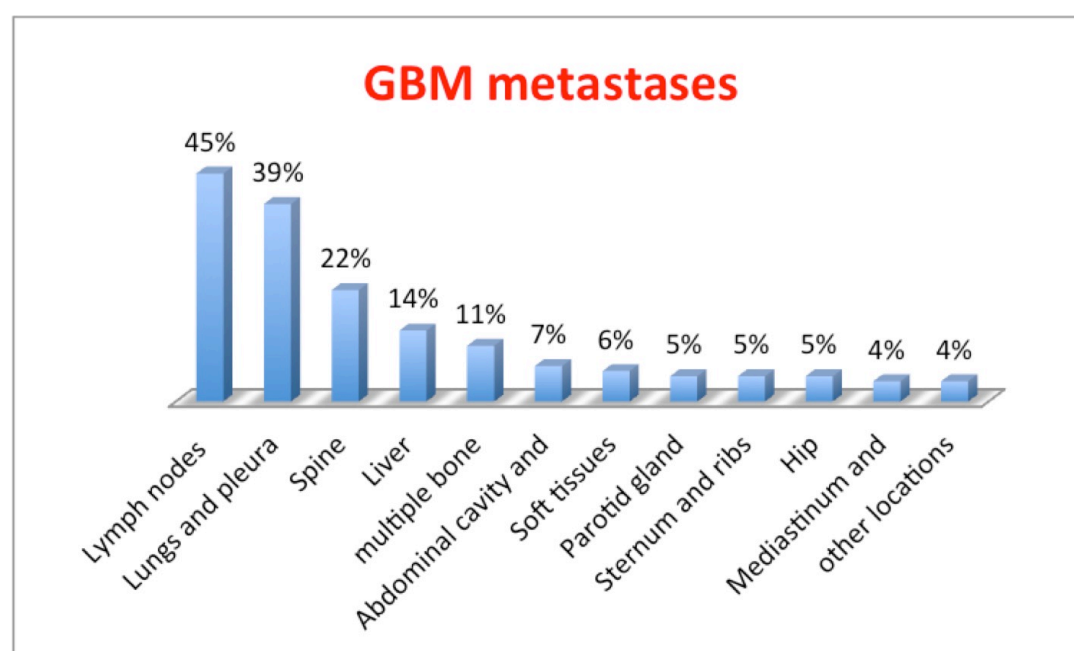
Historically, glioblastomas (GBM) were not believed to metastasize outside the CNS because of several reasons: low median survival, suppression of extracranial growth of GBM cells by the immune system, the absence of lymphatic channels in the CNS and the lack of specific receptors in the extraneural field. Therefore systemic radiological follow-up for metastatic spread is not a routine practice in most of the oncological center. We report a case of a metastatic GBM to the cervical spine presenting with a multilevel severe radiculopathy.

Case report

A 42-year-old man presented at our institution with a severe atrophic paresis of the deltoid and biceps. In 2012 he was diagnosed with occipital GBM, wild-type IDH1 and MGMT methylation and treated by three successive total resections, because of local recurrence, followed by fractionated radiotherapy and chemotherapy (temozolomide). In October 2015 a new local recurrence invading the superior sagittal sinus was diagnosed and treated with cyber Knife radiosurgery and concurrent introduction of Bevacizumab followed by a rapid regression in size of the lesion. At current admission spine MRI revealed a slightly enhanced tumor infiltration of the 3rd and 4th vertebra extending into the prevertebral and epidural space through the right C5 and C6 foramina. Whole-body CT and FDG-PET study showed multiple hypermetabolic pulmonary nodules. Needle biopsy confirmed the diagnosis of an extracranial metastasis from the cerebral GBM. Cyber-Knife fractionated radiosurgery of the C4 lesion was subsequently performed in march 2016 in a palliative intention along with chemotherapy with Bevacizumab.

Discussion and conclusions

148 cases of extraneural GBM metastases are reported and they occur in only about 0.2-0.4% of patients and their incidence correlates with previous neurosurgical intervention and long-term survival. 28 cases of patients with vertebral body metastases are reported in literature, they tend to occur in younger patients (mean age 38yrs) experiencing longer overall survival; the average length survival from diagnosis of spinal metastases was of 10 months. Since this tendency is expected to increase, long-term survivors should be evaluated for extraneural metastases in their routine follow-up. With increasing incremental gains in the survival of patients with GBM, clinicians will encounter patients with extracranial metastasis and early radiologic detection and treatment may improve quality of life.



Metastases distribution

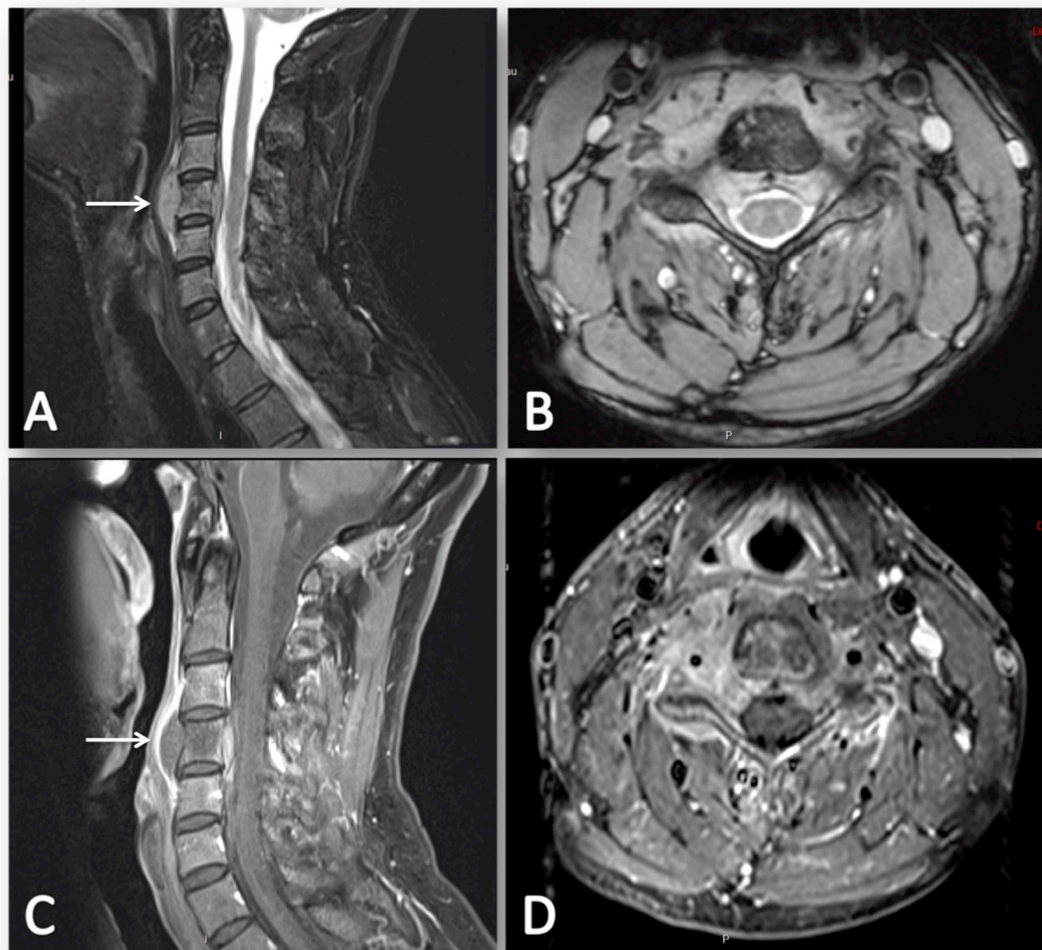


Fig.1

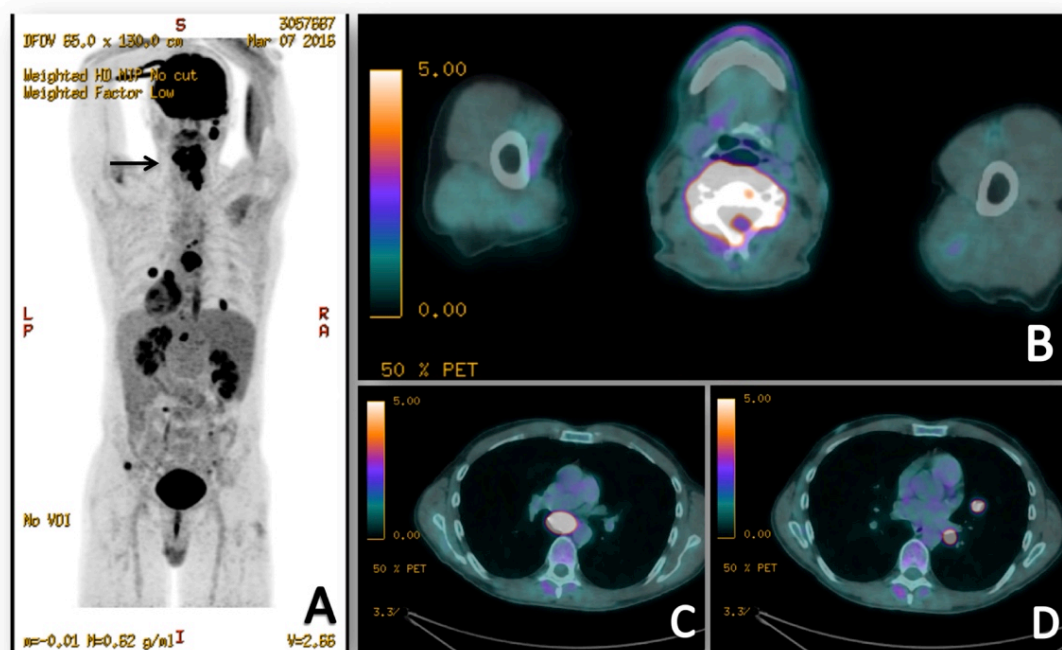


Fig.2

P97**Perfusion, diffusivity, ADC and susceptibility changes in meningioma after embolization.**

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Objectives

To investigate changes of tumor perfusion, diffusivity, effects on ADC and susceptibility in patients with intracranial meningiomas who underwent embolization using Embozene® particles prior to neurosurgical treatment.

Introduction

Meningiomas are the most frequently diagnosed primary extra-axial brain tumors. Most meningiomas are characterized by slow and insidious growth. In many patients symptoms which lead to meningioma detection are present at a stage of substantial tumor size. In that situation pre-operative embolization may facilitate surgery and decrease surgical complications due to decreased intra-operative bleeding, shortened surgical time, and easier resection. So far, there is no consensus on optimal timing for surgery after tumor embolization which is usually performed within few days after embolization.

Methods

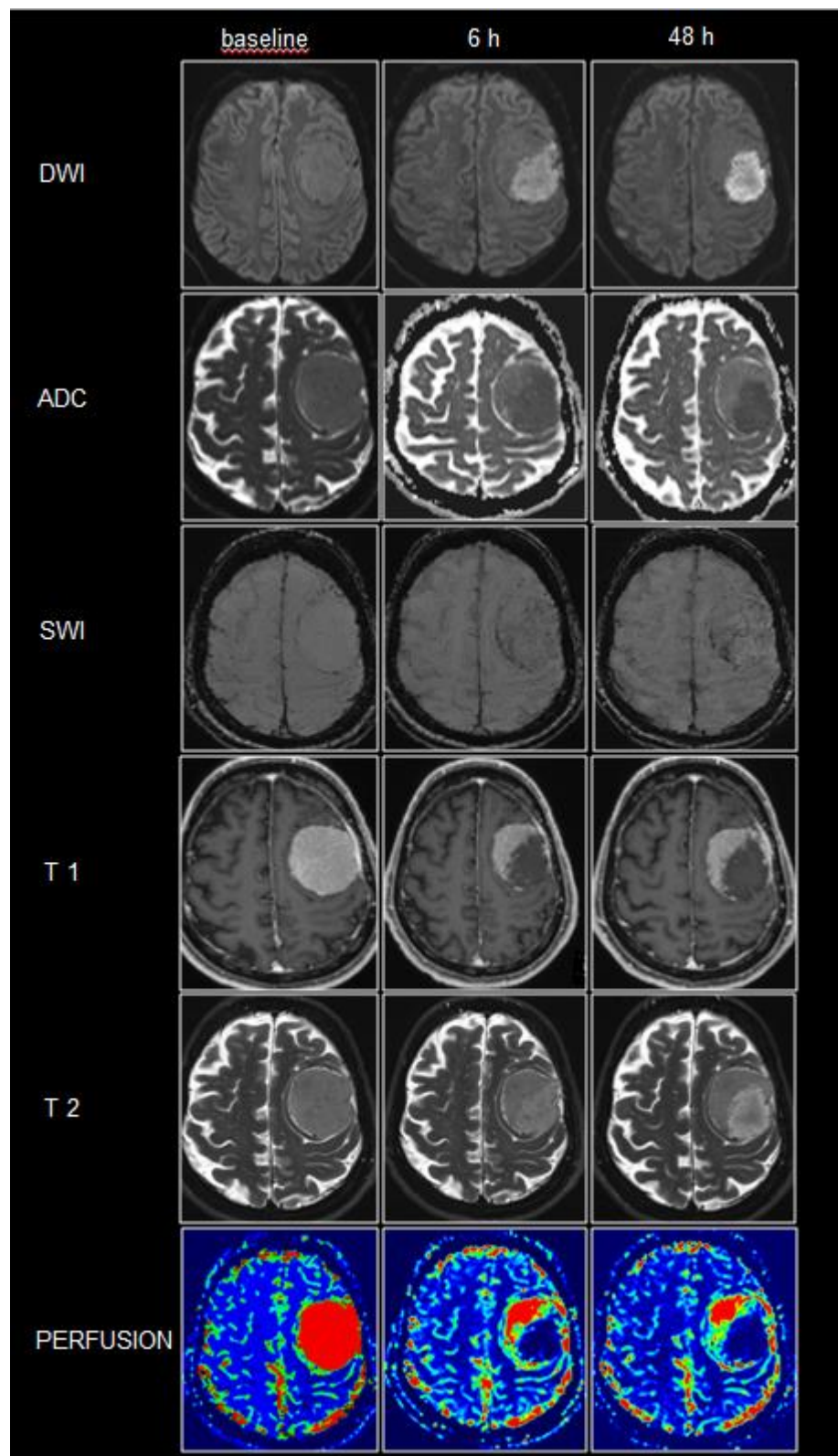
In this pilot study we enrolled patients with suspected meningioma based on magnetic resonance imaging (MR). Patients planned to undergo pre-operative endovascular tumor embolization followed by surgery were candidates for this study. Patients were scanned before embolization (baseline), and 6h and 48h thereafter. Pre- and post-embolization MR was analyzed for changes of tumor perfusion, diffusivity and effects of hypoxia/anoxia to ADC, as well as peri-lesional edema and microbleeds.

Results

Up to now 15 patients were prospectively included. In all cases the embolization remains subtotal due to partially fed of the tumor by the internal cerebral artery. The MR-hypoperfusion of the tumor shows a slightly increase from 6h to 48h after embolization. The detailed analysis of effect on diffusion and ADC is still outstanding. No relevant intra-tumoral micro-bleeds and no macro-hemorrhagic transformation occurred. Only 3 patients showed slightly uncritical peri-lesional edema after embolization. The surgeon observed reduced blood loss, easier surgical conditions and decrease of overall surgery time.

Conclusion

First data shows a successful embolization using Embozene® particles and resulting in benefits for the post-interventional surgical procedures. We could not observe any relevant intra-tumoral bleeding due to embolization. Tendentially it seems to be better performing the tumorresection 48h after embolization than 6h. Recruitment of further patients is still ongoing.



P98**Motor outcome of neonatal arterial ischemic stroke: Prognostic value of early neuroimaging**

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Background

Neonatal ischemic stroke is associated with cerebral palsy (CP) and cognitive impairment. Involvement of the corticospinal tract is known to be predictive for poor motor outcome. Aim of the study is to test the prognostic value of diffusion weighted images at stroke onset regarding CP symptoms 2 years after stroke.

Methods

We included 58 children (20 females) with a mean age of 2.2 ± 2.1 days at stroke manifestation. CP at 2 years were compared with lesion volume by using spearman correlations; infarct localization by using χ^2 tests and Odds Ratio.

Results

Of all children, 22 had CP. The infarct was bilateral in 24.1%, right sided in 20.3%, and left sided in 65.6% of the children. Laterality of stroke had no influence on 2 years outcomes. Volumetric data showed a correlation between stroke lesion volumes and motor outcome ($r=.551$, $p<.001$). The highest odds ratio regarding CP at 2 years post-stroke was found for the involvement of the thalamus and the basal ganglia. In the case of CP, involvement of thalamus and basal ganglia (lesion location) remained more predictive than lesion volume itself (Wald=5.519, $p=.019$, Exp(B)=16.0).

Conclusion

Early MRI in children with neonatal ischemic stroke has a prognostic value regarding clinical outcome two years after stroke. Lesion volume as well as lesion location are related to motor outcome. Moreover, if strategic brain areas are such as basal ganglia and thalamus are involved, lesion localization is more predictive than lesion volume regarding CP at 2 years follow-up.

P99**Computer Aided Radiological Diagnostics: Random Forest Classification of Glioma Tumor Progression using Image Texture Parameters derived from MRI ADC-Maps**

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Purpose

Despite the huge amount of information provided by an MR-examination, the initial diagnosis and grading of frequently extremely heterogeneous brain tumors by visual inspection remains a difficult task. It was hypothesized that texture parameter analysis in combination with advanced statistical classification algorithms can solve this task.

Methods

In tumor diagnostics the apparent diffusion coefficient (ADC) maps are used to differentiate regions with high cellular density from regions with tissue edema and normal tissue. Figure 1 above shows ADC-maps of grade I to IV glioma (recorded at 1.5T), illustrating the difficulty to diagnose the correct grade from this type of images. The mean ADC-value only not a robust predictor for glioma grade. It was hypothesized here that the quantification of the heterogeneity of glioma might be useful for brain tumor grading. For quantification of the tumors heterogeneity, histogram as well as co-occurrence based texture parameters were computed. For 84 patients suffering from glioma (10 grade-I, 23 grade-II, 20 grade-III, and 30 grade-IV) patients a total of 108 texture parameters were computed, each quantifying another aspect of the tumors heterogeneity, and stored into a database. This database was used to compute classifiers using the random forest classification algorithm, using the original Breiman implementation of random forest as implemented in R statistical programming language. Random forest is a so called ensemble classifier method, that builds multiple decision trees (the forest) from randomly selected subsets of covariates, in this case texture parameters. A classification (patient diagnosis) is performed by entering the tumor texture parameter dataset into all decision trees (i.e. the forest). The final classification result is obtained by majority voting.

Results

See Table 1.

Discussion

The information contained in the tumor heterogeneity of ADC-maps allows for glioma grading with a high level of accuracy (see Table). An interesting aspect of the results presented above is the fact that the more benign grade I, II gliomas can be distinguished from the malignant gliomas grade III and IV without the need of contrast agent. Conclusion – The combination of texture parameters derived from ADC-maps with random forest classification enables glioma grading on individual base, and can therefore be regarded as a step towards computer aided radiological diagnostics (CARD) of individual patients.

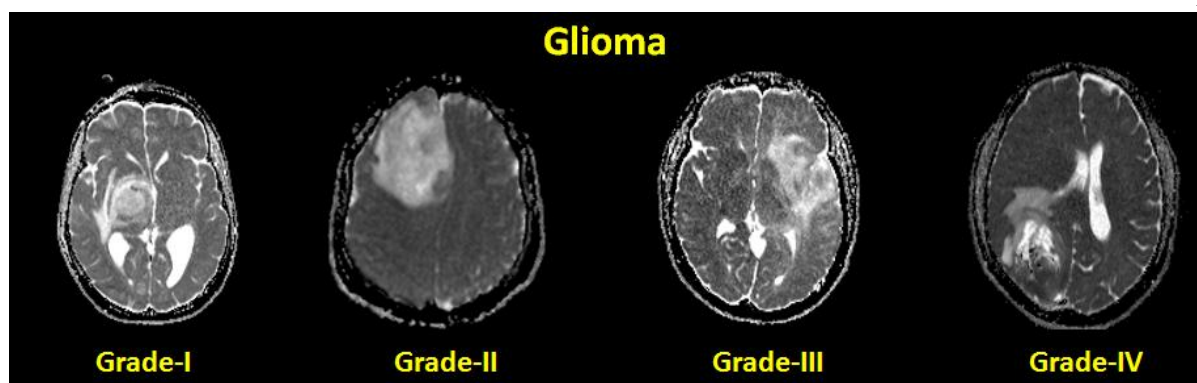


Table 1

Classifier Feature	Grade-I vs II		Grade-I vs III		Grade-I vs IV		Grade-II vs III		Grade-II vs IV		Grade-III vs IV	
	Grade-I	Grade-II	Grade-I	Grade-III	Grade-I	Grade-IV	Grade-II	Grade-III	Grade-II	Grade-IV	Grade-III	Grade-IV
Sensitivity	0.900	0.957	0.900	0.950	0.900	1.000	0.696	0.600	0.870	1.000	0.650	0.900
Specificity	0.957	0.900	0.950	0.900	1.000	0.900	0.600	0.696	1.000	0.870	0.900	0.650
Accuracy	0.939	0.939	0.933	0.933	0.975	0.975	0.651	0.651	0.943	0.943	0.800	0.800
Matthews correlation	0.865	0.865	0.860	0.860	0.933	0.933	0.541	0.541	0.889	0.889	0.580	0.580

P100**Flow dynamics of cerebrospinal fluid between the intracranial cavity and the subarachnoid space the optic nerve using an MRI diffusion sequence.**

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Purpose

Cerebrospinal fluid (CSF) nourishes the brain and removes toxic metabolites from the central nervous system. Impaired circulation of CSF is associated with optic nerve (ON) dysfunction in normal-tension glaucoma (NTG). At present, invasive computed tomographic (CT) cisternography is the only method available to demonstrate the relative penetration of contrast-loaded CSF into various CNS compartments and, thus, to observe CSF flow in the SAS of the ON [1]. It would be desirable to have a non-invasive method of observing CSF flow in the SAS surrounding the ON to eliminate the potential risks of CT cisternography as well as to expand its use in other conditions.

Methods

A modified magnetic resonance imaging (MRI) diffusion sequence was applied to quantify the flow in the subarachnoid space (SAS) surrounding the ON. To validate calculations, we used a phantom setup that consisted of a syringe pump creating a continuous flow of water inside through an intravenous line (Fig. 1). Clinical Image data was acquired of the right and left ONs and calculated a ratio between CSF flow in the ON and CSF flow in the brain (the flow range ratio, FRR) for 10 healthy subjects and 15 patients with NTG.

Results

For pooled data, the FRR from the healthy subjects was 0.63 ± 0.05 , with the range being similar for the right and left nerves ($p=0.1$). Statistically significant results were obtained ($p<0.05$) when comparing the FRR results of healthy volunteers ($n=22$ eyes, $FRR=0.63 \pm 0.05$) with the FRR of pathological eyes ($n=23$, 0.55 ± 0.08) of NTG patients (Fig. 2).

Conclusions

An optic nerve compartment syndrome can occur when normal CSF flow through the SAS of the ON is compromised. We have developed a non-invasive technique for assessing ON SAS flow dynamics that might present an alternative to computed tomographic cisternography.

References

[1] Killer HE et al. *Int ophthalmol clin* 2014.

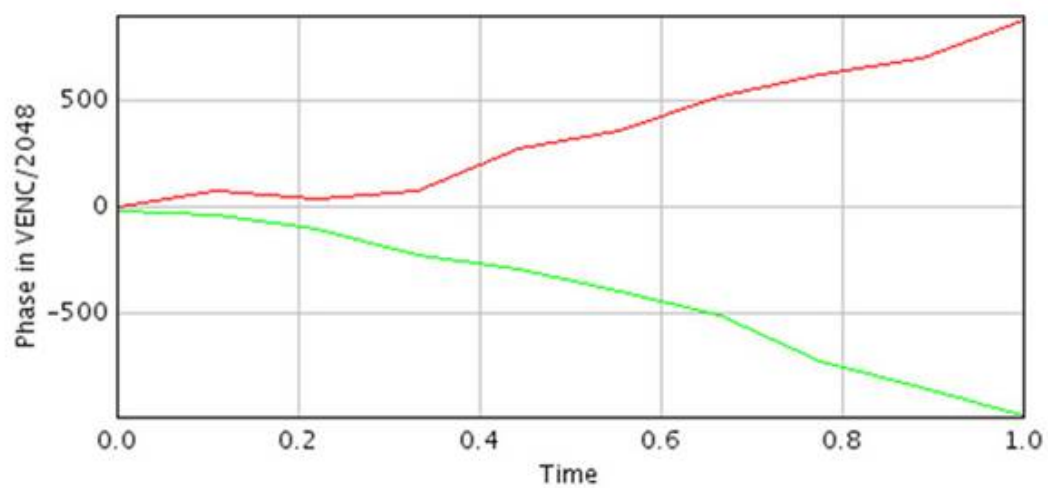


Fig. 1

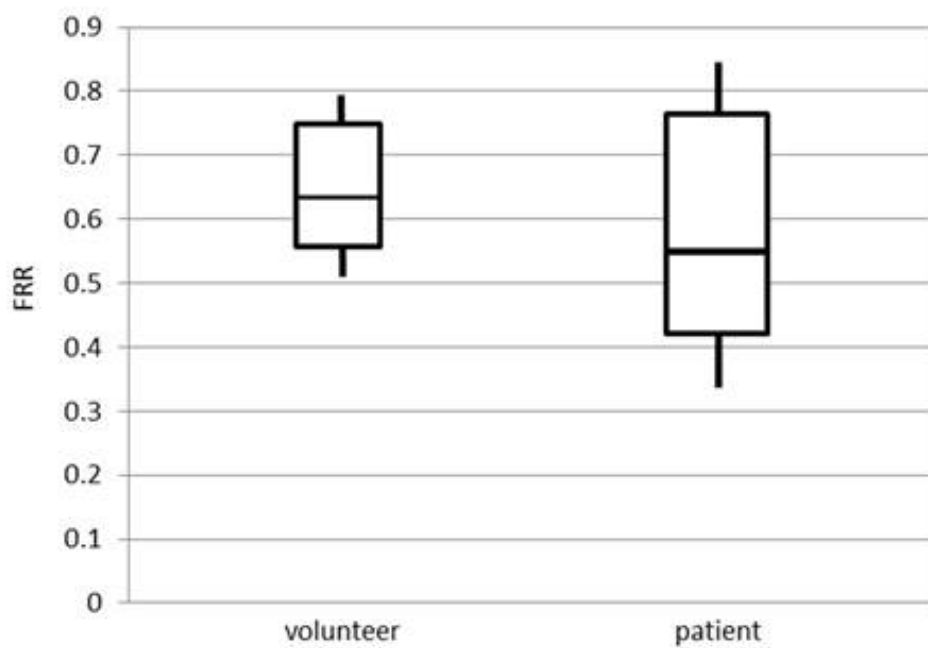


Fig. 2

P101**Reduction of Intracranial Clip Artifacts using Monoenergetic Extrapolations from Dual-Energy Computed Tomography**

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Purpose

To assess the value of monoenergetic extrapolations from dual-energy computed tomography (DECT) for metal artifact reduction of intracranial clips of various materials and sizes.

Materials and Methods

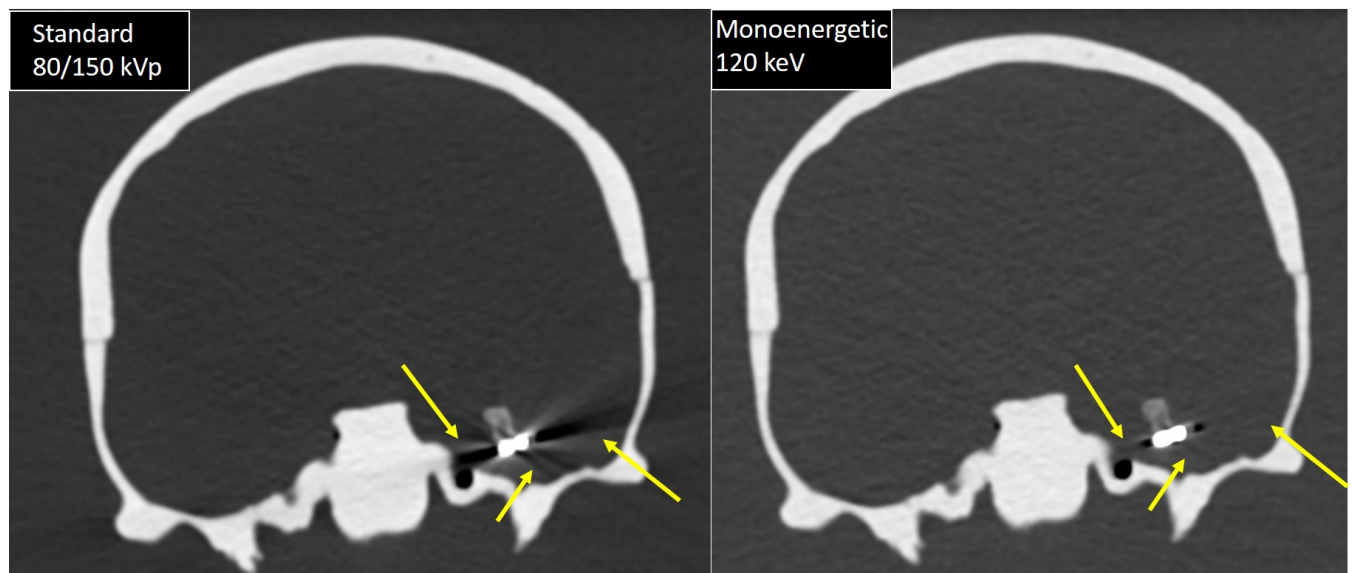
In this experimental phantom study, artifacts of six titanium clips (straight shape: size mini, small, medium and large; curved shape: size small and medium) and three Phynox (Cobalt-Chromium-Nickel alloy) clips (straight shape: size small and medium; curved shape: size medium) were examined using DECT scans. Postprocessing included routinely used standard 80/150 kVp mixed energy images and additional postprocessed monoenergetic extrapolations with 120 keV. Image analysis included the quantitative assessment of image artifacts (Hounsfield units [HU] measurements) as well as the qualitative evaluation of artifact severity and the visualization of contrast media filled adjacent simulated vessels using a four-point Likert scale.

Results

HU values of streak artifacts were significantly ($P < 0.05$) different between standard 80/150 kVp images (mean -228 ± 199 HU) and monoenergetic reconstructions (-2.1 ± 13.1 HU). Artifact scores improved significantly from 80/150 kVp images (median 3) to monoenergetic extrapolations (median 1; $P < 0.05$). Visualization scores of simulated vessels were significantly ($P < 0.05$) better with monoenergetic extrapolations (median 1) compared to 80/150 kVp images (median 2).

Conclusions

Monoenergetic extrapolations from DECT allow for a reduction of artifacts and a better assessment of clips and adjacent vessels compared to standard image reconstructions.



P102**Dual-Energy Computed Tomography in Stroke Imaging: Value of Virtual Non-Contrast Images for Detection of the Hyperdense Artery Sign**

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Background and Purpose

The hyperdense artery sign (HAS) in non-contrast CT is an early sign of thromboembolic arterial occlusion leading to ischemic stroke in the middle cerebral artery territory. This study investigated the value of virtual non-contrast (VNC) images derived from dual-energy CT (DECT) angiography for the detection of the HAS in patients with acute thromboembolic ischemic stroke using true non-contrast (TNC) scans as standard of reference.

Methods

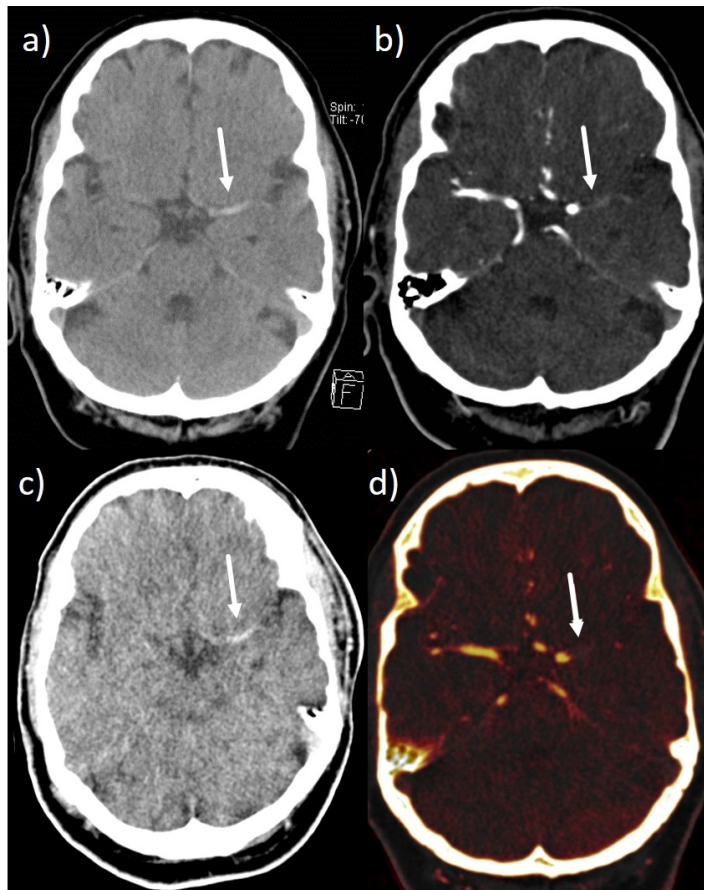
A total of 60 patients, either with acute ischemic stroke and HAS (n=30) or without HAS (n=30, control group) in TNC images were investigated. VNC images were post-processed from DECT angiography images. Clot presence and clot characteristics were assessed on VNC and compared to TNC images. Clot characterization included the level of confidence for the diagnosis of the HAS in VNC images, a qualitative clot burden score based on clot localization and extension, as well as quantitative clot attenuation [Hounsfield units; HU] measurements.

Results

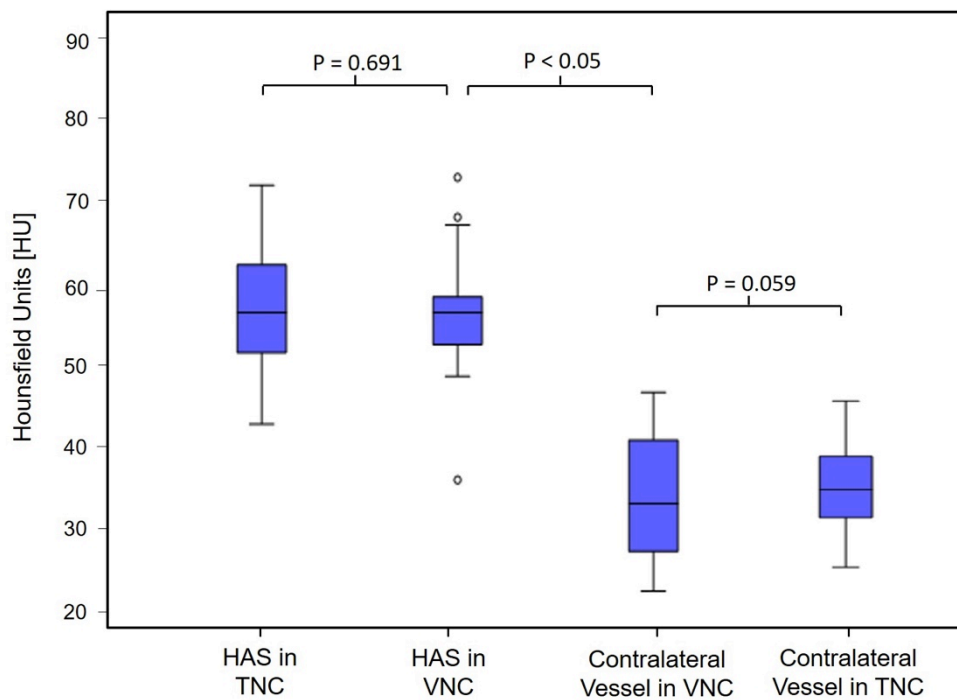
Sensitivity, specificity, and accuracy of VNC images for the diagnosis of the HAS were 97%, 90%, and 93%, respectively. No significant differences were found regarding the level of confidence ($P=0.18$) and for the clot burden score ($P=0.071$). Mean HU of the HAS in VNC images were higher ($56\pm 7.3\text{HU}$) compared to the contralateral, unaffected vessel ($33\pm 7.5\text{HU}$) ($P<0.05$). No significant HU differences were found among vessels with HAS in VNC ($56\pm 7\text{HU}$) and in TNC images ($57\pm 8\text{HU}$) ($P=0.691$).

Conclusion

VNC images derived from contrast-enhanced DECT enable an accurate detection and characterization of the HAS, potentially serving as alternative to TNC scans.



True non-contrast **(a)**, CT-angiography **(b)**, virtual non-contrast **(c)**, and iodine **(d)** images of a 71-year-old male patient with acute ischemic stroke. Images **(c)** and **(d)** are postprocessed images from **(b)**. The hyperdense artery sign is clearly visible in both **(a)** and **(c)** (arrow). Please note the vessel occlusion with the missing iodine contrast (arrow) in the CTA **(b)** and in the iodine images **(d)** compared to the contrast in the vessel on the contralateral side.



Quantitative results from CT attenuation measurements of the hyperdense artery sign (HAS) and the contralateral, unaffected vessel on true non-contrast (TNC) images versus virtual non-contrast (VNC) images.

P103**The GRASP Sequence - Neuroimaging of the Pituitary Gland**

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Aims

Report on advantages with the Golden-angle RAdial Sparse Parallel MRI sequence (GRASP) in patients with pathologies of the pituitary gland. The GRASP sequence combines the techniques of compressed sensing and parallel imaging for rapid continuous acquisition with the advantages of flexible spatiotemporal resolution using the golden-angle radial sampling scheme.

Methods

The GRASP sequence was implemented on 5 MR scanners (Prisma, Skyra, Verio, Avanto and Espree, Siemens Medical Solutions, Erlangen, Germany). The parameters were: TR/TE 4.42/2.13 msec, image matrix 256 x 256 mm, voxel size 1.0 x 1.0 x 1.0 mm, temporal resolution 4 s, TA 4:07 min. Images were read by two neuroradiologists with respect to delineation of pathologies and artifacts. Data were compared to standard T1w post CE and standard dynamic T1w post CE measurements.

Results

40 patients were retrospectively included. 7 patients were healthy. 33 patients had the following reports: preoperative macroadenoma (10x), postoperative makroadenoma (8x), microadenoma (9x), cyst (3x); craniopharyngeoma (1x), infarction (2x). In the GRASP sequence arrival of contrast media and distribution over time was well visible in all patients with additional high regional resolution. Both readers evaluated all pathologies in detail. Image quality was assessed comparable to standard sequences. Pulsation artefacts were not observed.

Conclusions

With the GRASP sequence all pituitary pathologies were well visible by simultaneously providing high temporal and high spatial resolution. We assume that a significant reduction of examination time will be achieved for these patients in the future by using the GRASP technique.

P104**Tirofiban versus aspirin ± clopidogrel in patients with urgent stenting for acute symptomatic carotid stenosis – Risks and benefits**

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Background and purpose

Emergent stenting of carotid artery stenosis necessitates the use of antiplatelet therapy to prevent in-stent thrombus formation. In case of hemorrhagic complication or need of surgery, an adequate thrombocyte function is necessary though. With its short action time, the GPIIa/IIIb antagonist Tirofiban may be a good alternative to the irreversible thrombocyte inhibition by Aspirin and Clopidogrel. We analyzed the safety and outcome of Tirofiban therapy in patients with emergent stenting of symptomatic carotid artery stenosis.

Methods

A series of 33 consecutive cases with acute symptomatic carotid stenosis that received endovascular treatment and antiplatelet therapy was retrospectively analyzed. Nine of them were initially treated with Aspirin, two of them additionally with Clopidogrel. The other 24 received initial treatment with Tirofiban. Bleeding complications with inclusion of several possible impact factors and clinical outcome were evaluated in both groups.

Results

There were 13 intracranial bleedings, 8 out of them were symptomatic intracerebral hemorrhages. Three of the 8 patients died. There was no statistical significance of the incidences between the two study groups (for intracerebral bleedings: OR 1.41; 95% CI 0.23 – 10.86, for sICH: OR 0.54; 95% CI 0.07 – 4.49). At three months, 6 (18.8%) patients had mRS of 0-1 and 11 (34.4%) a mRS of 2. No statistical significant difference was observed between the two groups ($p = 0.682$) regarding mRS.

Conclusion

There was no increased incidence of hemorrhagic complications under Tirofiban therapy, leaving it as a reliable alternative to other thrombocyte inhibitors, especially in patients with high probability of need for urgent surgical intervention.

P105**Evaluation of Intracranial Tumors with the 4D GRASP Sequence at 1.5 T and 3.0 T**

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Aim

Report on advantages with the Golden-angle RAdial Sparse Parallel MRI sequence (GRASP) in patients with intracranial tumors. The GRASP sequence combines the techniques of compressed sensing and parallel imaging for rapid continuous acquisition with the advantages of flexible spatiotemporal resolution using the golden-angle radial sampling scheme.

Materials and Methods

The GRASP sequence was implemented on 5 MR scanners (Prisma, Skyra, Verio, Avanto and Espree, Siemens Medical Solutions, Erlangen, Germany). The parameters were: TR/TE 4.42/2.13 msec, image matrix 256 x 256 mm, voxel size 2.0 x 1.1 x 1.1 mm, temporal resolution 3.5 s, TA 4:07 min. Images were read by two neuroradiologists with respect to delineation of pathologies and artifacts. Data were compared to standard 3D MPRAGE post contrast media application.

Results

By now 22 patients were retrospectively included. The reports were as follows: glioma (10x), lymphoma (1x), metastasis (3x), meningioma (5x), vestibular schwannoma (3x). All pathologies were correctly detected by the readers. Image quality was judged at least comparable to standard 3D T1w images, especially appreciated was the possibility to see distribution of contrast media over time and measurement of enhancement pattern in all pathologies with additional high regional resolution. Pulsation artifacts were not observed. The sequence served also for calculation of detailed permeability maps.

Conclusions

With the GRASP sequence all intracranial tumors were well visible by simultaneously providing high temporal, high spatial resolution and also providing the possibility to calculate permeability maps. We startet a prospective study and assume that we can significantly shorten scanning time in the future.

P106**Short-term effect of escitalopram on efficiency of sensorimotor networks**

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Introduction

It is known that serotonin is exerting both short- and long-term facilitatory effects on glutaminergic neuronal transmission. Recently clinical evidence that motor recovery from stroke may be facilitated by selective serotonin re-uptake inhibitors. (SSRI). The aim of the study was to measure the effect of a single dose of 20 mg escitalopram 3 to 4 hours after ingestion on the blood oxygenation level dependent (BOLD) signal by er-fMRI during tactual object manipulation. We expected signs of enhanced synaptic efficiency after escitalopram medication deduced from a differentiated expression of sensorimotor networks evoked by tactile manipulation of objects.

Methods

10 healthy right-handed volunteers were included into the study. The study received ethical approval from both research centers. All participants gave written informed consent before enrollment. During fMRI acquisition, subjects had to manipulate a non-magnetic cube, which was presented to the subject's right (dominant) hand. One run (total duration 7.4 min.) consisted of 24 presentations, one presentation lasted 6 s, intervals between object presentations varied pseudorandomly between 10 and 14 s. fMRI experiments have been conducted in two sessions, once with placebo and once 3-4 hours after ingestion of 20 mg escitalopram (mean interval 14 days). The order of the trials with placebo and escitalopram was pseudorandomized. On the pre-processed fMRI time-series data principal component analysis (PCA) related to the paper of Kägi et al.¹ was executed using in house software written in Matlab based on the algorithm described by Alexander and Moeller². The component of each acquisition yielding the maximum volume correlation coefficient with the maximum correlation coefficients (ecc) of the present study was used to determine the mean condition images and the paired difference image. Salient principal component images were selected, i.e. with 99 percentile amplitude thresholds and 32 voxel minimum and for negative ecc, 01 percentile.

Results

Median age of the subjects (5 m, 5 f) was 63, range 50 to 67. The mean condition image placebo and verum with 99 percentile amplitude threshold and 32 voxel minimum showed both clusters pre- and postcentral gyrus and supplementary motoric area on the left side and precentral gyrus in the right side (meanweight1). The mean condition image with 01 percentile amplitude threshold exhibits clusters in the inferior parietal lobule, medial prefrontal area.

P107**Kawasaki Disease with Central Nervous System Vasculitis: a rare association**

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Background

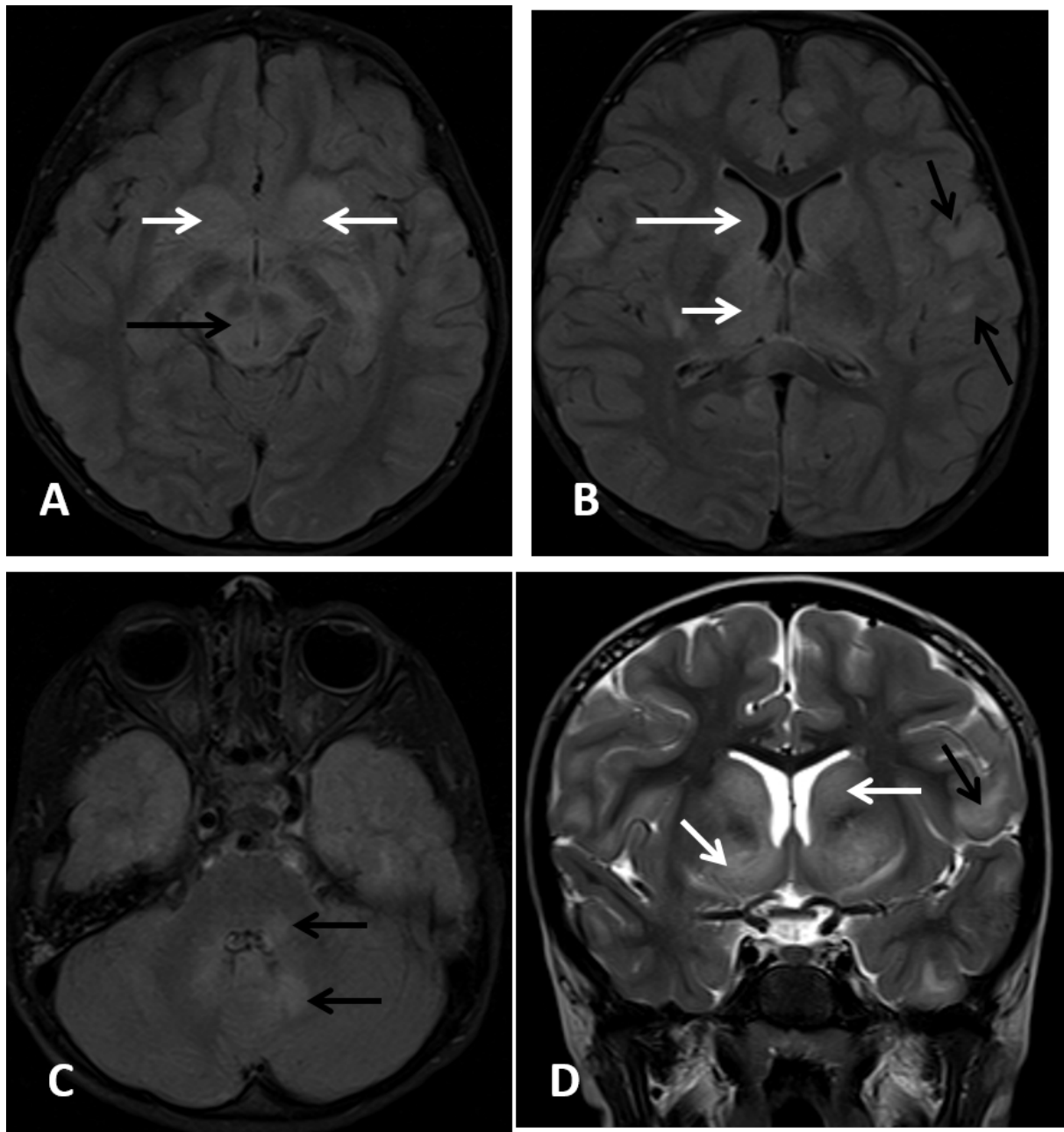
Kawasaki disease (KD) is an acute vasculitis of unknown etiology with varied clinical manifestations. Central Nervous System (CNS) involvement occurs in 0.4% of children. The manifestations are diverse; ranging from a headache, seizures, chorea, changes in personality, depression, memory and concentration problems, cognitive impairment, cerebrovascular accidents to coma, and death. CNS vasculitis is not frequent in pediatric age group and could be primary or secondary to collagen vascular disorders, malignancies, infections, Behçet's disease or be related to drugs. Few reports describe the association of KD with CNS vasculitis.

Case report

A 5-years-old female presented with fever for seven days followed by a decrease of activity and oral intake, subsequently, she had redness and swelling of the palm and sole associated with feet pain which was severe enough to affect her walking. Her mother noticed skin peeling on the tip of fingers shortly after the erythema along with bilateral nonpurulent eyes redness. At the tenth day of her illness, the mother found her unresponsive and developed convulsion that lasted for 20 minutes and aborted in the emergency department by lorazepam. She was treated with antibiotics and acyclovir for suspected meningoencephalitis. However, she continued to have a fever with persistent high inflammatory markers and she has transient mild anterior uveitis. Brain magnetic resonance imaging (MRI) showed; Swollen high T2 and FLAIR signal intensity at bilateral basal ganglia, thalami, and midbrain. Multiple small lesions of similar signal intensity at cerebellum left middle peduncle and cortical/sub cortical areas. Incomplete Kawasaki disease with CNS vasculitis was suspected. She was started on IVIG 2 g/kg, the girl's fever resolved along with other vasculitis features. Also she received steroid 2 mg/kg/day and tapered over 3 months and also given Carbamazepine. Her subsequent follow-up in outpatient visit showed complete resolution of her symptoms and repeated MRI Brain showed complete resolution of previously noted lesions.

Conclusion

Early recognition of severe or unusual forms of Kawasaki disease could lead to the more favorable outcome by using appropriate treatment strategies. Brain MRI features might be a key sign for the diagnosis of medium or small cerebral vessel involvement. Only a few cases of KD with CNS vasculitis has been reported.



P108**Episodic memory network in very preterm-born children**

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Very preterm-born children are at risk for lower levels of cognitive performance including reduced memory capacity. Given the centrality of episodic memory for learning and school achievement and given its susceptibility for impairment, it is critical to understand how episodic memory is represented in the child's brain.

The aim of this study was to examine the episodic memory network during encoding and recognition and to determine the effect of age and memory performance on the episodic memory network in very preterm-born and term-born children.

Brain activation during fMRI was examined using a block-designed verbal episodic memory task in 40 very preterm-born and 34 term-born children aged 7 to 12 years. Children had to memorise and later recognize visually presented word pairs in the scanner and performed a verbal memory task outside the scanner. In very preterm-born children, the frontal encoding network and the fronto-parietal recognition network were more extended than in term-born children. During encoding and recognition significantly more activation occurred in left-sided language processing areas (angular gyrus, middle temporal gyrus) in preterms than controls. During encoding and recognition there was an overlap of activations in left frontal brain regions in preterms but not in term-born children, confirming the reinstatement hypothesis at least in the preterm group. Age and episodic memory performance was not conclusively associated with the episodic memory network, neither in preterm-born nor in term-born children.

The results of this study revealed that preterm-born children recruit a more extended frontal network during encoding and a more extended fronto-parietal network during recognition than term-born children. This might reflect different pathways of processing episodic memory information in preterm-born children.

P109**Grey matter changes after treatment of carotid artery stenosis**

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Background

Treatment of carotid artery stenosis (CAS) decreases the long-term risk of stroke and may enhance cerebral blood flow. It has the potential to prevent cognitive decline and improve cognition over the long-term. However, exact neural mechanisms of treatment and their impact on cognitive recovery remain unclear.

Objective

To investigate morphometric long-term effects and cognitive recovery one year after treatment.

Method

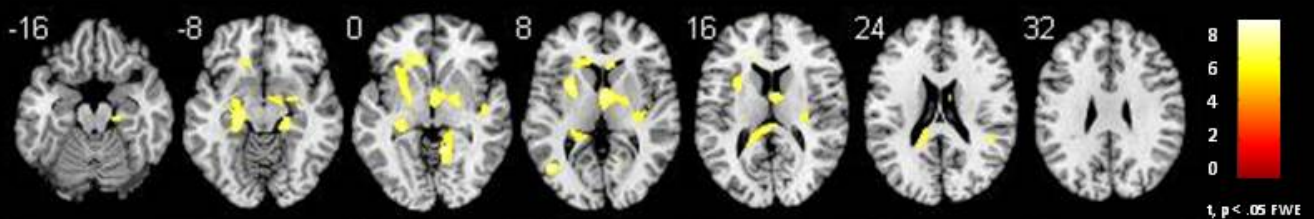
To detect areas with longitudinal grey matter (GM) volume change, we performed tensor-based-morphometry of MRI data acquired before and one year after treatment in 25 patients with CAS. GM changes were correlated with cognitive gain scores published earlier.

Results

GM volume expansion after treatment was found in medial areas of the motor system. Improvement in executive function was related to GM expansion in the bilateral prefrontal cortex and improvement in visual episodic memory was related to increased GM in left parietal cortex.

Conclusion

Surprisingly, no decrease of GM volume was found after treatment. However, GM volumetric expansion occurred after treatment in areas of the motor network, suggesting better interhemispheric connections. Morphological changes are furthermore related to cognitive improvement after treatment.

Grey matter volume change

Stenosis side flipped to right hemisphere. Results covaried for age, gender and total intracranial volume.

P110**Domain Specific Analyses of Cognitive Changes in Patients with Parkinson's Disease – Results of a 3-Years Follow up Study**

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Background and Aims

The exact course of cognitive decline in Parkinson's disease (PD) patients is under discussion. We aimed to examine the frequency and the profile of cognitive changes in non-demented PD patients over 3 years. Methods Fifty-three PD patients were evaluated with neuropsychological tests at 4 distinct time points (baseline, 4 weeks, 6 months, 3 years) covering five domains (attention, working memory, memory, executive function, visuo-construction). Wilcoxon and Fisher's test were used to compare clinical features of patients with and without progression. The course of cognitive decline was analysed using ANOVA with repeated measures.

Results

In the still ongoing study, after 3 years, 26 patients had remained cognitively stable (21 cognitively normal; 5 PD-Mild Cognitive Impairment (MCI)), 6 had progressed to PD-Dementia (PD-D) and 4 to PD-MCI. At baseline, patients with a progression were significantly older ($p<.05$), had more severe motor signs ($p<.05$), higher education ($p<.05$), and their relatives indicated a significant decline in cognitive functioning (IQCode: $p<.05$) than those who remained cognitively stable. 26 patients have been fully investigated with the comprehensive neuropsychological test battery at 4 time points. ANOVA showed a significant effect of time in the memory domain ($p<.0001$). Post-hoc testing revealed a significant decline from baseline to 3 years ($p<.001$). No significant decline in the other domains was detectable.

Conclusions

In this sample of PD patients, cognitive decline over the course of 3 years is mostly seen in the memory domain. A decline in the memory domain might be an important marker for the prediction for PD-D.

P111**Investigating the Serial Position Effect in Verbal Memory in Patients with Parkinson's Disease (PD) - a Longitudinal Study**

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Background & Aims

Serial position (SP) effect describes that the first (primacy) and last (recency) items of a word list are remembered better compared to the middle items. Especially, the primacy effect is diminished in PD patients. The aim of this study is to investigate the time course of the SP effect in PD patients.

Methods

25 PD patients (66y [51-75], education: 14y [9-20], gender: 15M, 10F, disease duration: 5y [1-19], L-Dopa: 400 [1-1100]) were tested with the Basel Verbal Learning Test (BVLТ) at baseline, after 6 months and 3 years. The first and last two words of the list were defined as the primacy and recency words, respectively. For statistics we used repeated measures ANOVA and general linear models (GLM) and corrected for age, gender, education, medication, and PD-onset).

Results

PD patients remembered recency words better than primacy ($p < 0.001$), whilst middle positioned words were rarely recalled ($p < 0.001$). There was a significant interaction between SP and time ($p < 0.001$). There, PD patients remembered recency words better than Primacy ($p < 0.001$), overall performance was better at 6 months compared to baseline, and 3 years. The only significant confounding factor was age ($p < 0.005$).

Conclusions

Analysis of the SP effect in PD patients over time might hint at slower semantic processing compared to phonological processing.

P112**Capacity of Odour Identification in Patients with Parkinson's Disease (PD) Correlates with Aspects of Executive Function, but not Motor Impairment**

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[1] University Hospital Basel, Basel, Switzerland

Background

The decline of olfaction has been identified as an early symptom of Parkinson's disease (PD) and often precedes the manifestation of specific cognitive deficits, especially in the executive function domain. Here, we investigated whether decline in odour identification in patients with PD correlates with cognitive decline as measured in neurocognitive tests for executive function and with motor impairment.

Methods

We investigated 67 PD patients (47 male, 20 female), mean age 66.9 (± 9.47) years, assessed with tests for executive function (Wisconsin Card Sorting Test (WCST), Trail Making Test, semantic and phonemic fluency, working memory) and for odour identification. As a measure of motor impairment UPDRS III was applied; furthermore, levodopa dosage (LED) was calculated. In order to control for age effects, all variables that entered analysis were corrected for age. For statistical analysis, we calculated Spearman's rank correlations.

Results

As expected, PD patients showed a significant reduction in odour identification for all olfactory stimuli compared to the healthy age-matched validation sample ($p < 0.001$). Reduced working memory performance was the only variable significantly associated with decline in odour identification ($p = 0.018$). For the WCST we found a trend association with odour identification ($p = 0.08$). No other measures of executive function and motor impairment (UPDRS III, LED), showed a statistically significant correlation with odour identification (all $p > 0.11$).

Conclusion

In our sample of PD patients olfactory decline is associated with some cognitive tests assessing executive function, while there is no correlation with severity of motor symptoms.

P113**Combined intensity ratings of congruent and incongruent facial emotions highly discriminate between behavioral-variant frontotemporal dementia and major depressive disorder**

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In its early stages, behavioral-variant frontotemporal dementia (bvFTD) is frequently misdiagnosed as major depressive disorder (MDD) due to overlapping symptoms. Recent studies have revealed the potential of emotion processing paradigms for improving the differentiation between the two diseases. The current study compared 25 bvFTD patients, 20 MDD patients, 21 Alzheimer's disease dementia patients, and 31 healthy controls on a novel emotion intensity perception task. Participants were asked to rate the intensity of morphed faces from the Ekman and Friesen stimulus set on the congruent emotion (i.e., sad stimulus and rating on sadness) and on the five incongruent basic emotions (i.e., sad stimulus and separate ratings on anger, disgust, fear, happiness, and surprise). In contrast to the other groups, bvFTD patients misrecognized emotions, in particular negative emotions. MDD patients showed a negative response bias for congruent negative facial emotions, but not for incongruent negative facial emotions. Although both ratings of congruent and incongruent negative facial emotions differentiated well between bvFTD and MDD, the highest discrimination between the two diseases was achieved by combining both types of rating. This emotion intensity perception task, which is easy to administer in the clinic, appears to be a valuable tool to discriminate between early bvFTD and MDD patients, and therefore to improve the diagnostic accuracy of bvFTD

P114**A new Serious Game based multitasking assessment tool for cognition and activities of daily living**

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Developing easy, short and ecological diagnostic tools for prevention of Alzheimer's disease is of major importance because of the constant evolution of this disease. These tools need to be representative of reality as patients can encounter problems in laboratory tests whereas they don't notice any problems in daily living activities. Multitasking is present in everyday instrumental activities of daily living and was recognized as a main factor for rehabilitation process and for independent life at home. However, the use of multitasking in diagnostic tool remains rare, due to the difficulties of implementing in laboratory setting. The aim of the present study was to develop and evaluate a new multitasking based assessment tool for cognition and daily living activities and to compare the performances with a real cooking task. Eighteen healthy participants between the ages of 66 and 84 (mean age = 74.6, SD = 6.126 years) were recruited through the Senior University of Bern.

All participants were assessed with a standardized neuropsychological test battery and performed a virtual cooking task and a real cooking task, which were comparable in terms of utensils and ingredients needed and task demands (i.e. to prepare a plate of spaghetti with tomato sauce). To compare the equivalence of reliability measures between the virtual and real cooking task, the two reliability coefficients were tested for significant differences using the Fisher-Bonett test for small samples. A Pearson correlation matrix was computed to evaluate whether single domain can correlate with the cooking performance in the Serious Game. Convergent and divergent validity was carried out using multiple regression analysis. The Fisher-Bonett Test revealed no significant difference in the alpha coefficients between real and virtual cooking task. Pearson correlation analysis showed no significant single domains correlated with the performance in the Serious Game. However, the model of neuropsychological performances as predictors of the virtual cooking performance was statistically significant. Prospective memory, executive functions and visuo – spatial orientation were good predictors of the performance of the virtual cooking completion and performances in the virtual cooking task were good predictors for performances in the real cooking task. The new Serious Game based multitasking assessment tool is an ecological way to evaluate cognitive abilities.

P115**Mental toughness, sleep disturbances, and physical activity in patients with multiple sclerosis (MS) compared to healthy adolescents and young adults.**

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Background

Multiple Sclerosis (MS) is the commonest chronic autoimmune demyelinating and inflammatory disease of the central nervous system, afflicting both body and mind. Typical symptoms are fatigue, paraesthesia and depression, along with cognitive impairments. Further, the risk to suffer from MS is 2.5 to 3.5-fold higher in females compared to males. Whereas there is extant research on fatigue, depression, and cognitive impairment of patients with MS during the clinical course, no research focused on sleep, psychological functioning, and physical activity at the time point of diagnosis.

The aims of the present study were therefore to assess possible state markers of mental toughness as a dimension of psychological functioning, sleep disturbances, physical activity among patients at the moment of the diagnose, and to compare these data with those of healthy adolescents and healthy young adults.

Methods

A total of 23 patients with recently diagnosed MS (mean age: $M = 32.31$ years; 91% females), 23 healthy adolescents (mean age: $M = 17.43$ years; 82% females), and 25 healthy young adults (mean age: $M = 20.72$ years; 80% females) took part in the study. They completed a booklet of questionnaires covering socio-demographic data, mental toughness, sleep disturbances, and physical activity.

Results

Patients with MS reported similar mental toughness traits as adolescents, and an equal amount of moderate physical activity and sleep disturbances as young adults. Further, patients reported a lower level of vigorous physical activity, compared to both healthy adolescents and young adults.

Conclusions

Compared to healthy adolescents and young adults, patients at the moment of their diagnosis of MS reported similar mental toughness traits, sleep disturbances and levels of moderate physical activity. The pattern of results of the present pilot study suggests that the onset of MS is not predictable by poor mental toughness, poor sleep, and decreased moderate physical activity.

P116**Stressful life events during pregnancy: impact on mother's and off-spring's postnatal health, indexed by prenatal steroid hormone deposits in maternal hair strands and infant nail clips**

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Objectives

Severe stress exposure (SE) during pregnancy may affect mother's and off-spring's well-being in postpartum period. The aim of this study was to examine, if stressful life events during pregnancy were associated with subsequent postpartum depression (PPD), specific pregnancy outcomes and infant irritability at 3 months p.p. Further we explored if such stress related outcomes could be indexed by retrospective means of maternal hair and infant nail steroid hormone analyses.

Methods

In a prospective study, 79 healthy mothers at time of delivery rated stress exposure by life events during pregnancy and degree of postpartum depression at 3 months p.p. with questionnaires. Mother-infant dyads with during pregnancy were compared to others with low stress exposure. Maternal hair strands corresponding to 3rd trimester and 3 months p.p. as well as newborns' nail clips were collected. Steroid hormone concentrations in hair and nail samples were assessed with tandem liquid chromatography mass spectrometry analysis. Pregnancy outcomes were derived from obstetrical records.

Results

1) Mothers with SE during the 2nd or 3rd trimester reported increased postnatal depression scores. Further, they had decreased hair cortisone levels in their prenatal hair segment. Moreover, decreased prenatal hair cortisone and increased hair cortisol/cortisone ratio correlated with increased postnatal depression scores.
2) In off-springs exposure by SE in 1st trimester was related to increased infant irritability at the age of 3 months, and this association was related to increased Dehydroepiandrosterone (DHEA) levels in infants' nail clips. Moreover, both, exposure to SE in 3rd trimester and increased prenatal maternal hair cortisol/cortisone ratio were associated with increased cortisol in infant nail clips which correlated with and decreased birth weight.

Conclusions

Exposure to SE during pregnancy affects both, mothers and off-springs. Mothers bear an increased risk for PPD, whereas their off-springs present with more irritability after early pregnancy SE, and with decreased birth weight after late pregnancy SE. These associations seem to be mediated by alterations of hypothalamic-pituitary-adrenal axis, as reflected by retrospective maternal hair and infant nail steroid analyses. If validated in further studies, retrospective hair and nail steroid analyses might serve as valuable risk indicators of stress associated health problems of mothers and off-springs.

P118**Aerobic Exercise as Add-on Treatment in Depressed Inpatients Improves Cognitive Symptoms but not Symptom Severity**

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Purpose of the study

Aerobic exercise seems to have medium effects on symptom severity in mild to moderate depression[1]. Additionally, there is evidence on positive effects on cognitive symptoms[2]. However, data supporting this hypothesis are still scarce. Since cognitive symptoms of depression are difficult to treat by antidepressants, novel treatment options for cognitive complaints are urgently needed. Thus, we started this project to evaluate the effect of aerobic exercise on cognitive variables in depressed inpatients.

Methods

Inpatients with a diagnosis of depression (first episode, recurrent and bipolar) and a score >16 in the 17 item Hamilton Depression Scale (HDRS-17) were randomly assigned to either endurance exercise on indoor bicycles (17.5kcal/kg/week) at 60-75% of maximal heartrate (approx. below the anaerobic threshold) or a standardized stretching and coordination program 3 times per week for 6 consecutive weeks as add-on therapy to multimodal antidepressant treatment. Patients were recruited on the depression wards of the Psychiatric University Hospital Basel, Switzerland and the Psychiatric Services Solothurn, Switzerland between October 2013 and February 2016. HDRS-17, alertness and working memory were measured before (baseline) and after (TP2) the intervention. Cognitive variables were measured with the TAP-test V. 2.3. Since not all data met criteria for parametric tests, non-parametric tests were used to calculate time-effects and between-group differences.

Results

17 female and 16 male patients with a mean age of 37.9 (± 13.1) were recruited into the study (17 controls, 16 intervention group). Three had a diagnosis of bipolar depression, 15 recurrent depression and 15 first MDD: At baseline, there were no significant group-differences for demographic variables, HDRS-17 and cognitive variables (Chi2, Mann-U-Whitney-test). Mean HDRS-17 was 21.4 (± 3.6). After 6 weeks, mean HDRS-17 decreased significantly to 8.6 (± 6.7) in both groups with no group difference. At TP2, median reaction time for working memory was significantly lower in the intervention group 508.8 (± 133.1) vs. 622.0 (± 152.2) in controls (Mann-U-Whitney-test $p=.037$, $r=.36$). Alertness with warning signal showed a trend to a group difference between intervention 32.2 (± 19.1) vs. 37.5 (± 14.8) in controls. We also found a trend for a time effect in working memory for the intervention group between TP1 and TP2 (mean difference: -62.1, $p=.093$, $r=-.42$, Wilcoxon rank-sum test), the control group showed no trend over time (mean difference: 37.7, $p=.136$, $r=.36$).

Conclusions

Aerobic exercise as an add-on treatment to a multimodal program for depressed inpatients seems not to have additional effects on symptom-severity. However, this may be due to ceiling effects because of a very effective multimodal treatment regime and overlapping effects. However, despite the relatively small sample size of this study, aerobic exercise showed to have medium effects on reaction time in working memory. Therefore, regular exercise may contribute to an improved course of cognitive symptoms among clinically depressed patients.

Disclosure

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P119**Visually detected nrem-s2 sleep spindles of five year old kindergarten children correlated with more prosocial behavior at baseline and one and four years later**

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Objectives

Sleep electroencephalogram (EEG) spindles are associated with efficient cortical-subcortical connectivity, and intellectual and learning abilities. Moreover, in a previous study (1), visually detected NREM-S2-spindles of five year old kindergarten children were correlated with emotional/behavioural characteristics cross-sectionally and at follow-up one year later. Now, we present follow-up data of the same cohort at the age of nine years. Our aim was to examine, if NREM-S2-spindles of five year olds would predict even longer trajectories of emotional/behavioural development.

Methods

A total of 43 children at five years of age underwent objective sleep-EEG monitoring in their homes. Emotional and behavioural dimensions were assessed by parents and teachers with the Strengths & Difficulties Questionnaire (SDQ) at baseline, and at the age of 6, and 9. NREM S2 spindles were visually scored and compared with SDQ dimensions.

Results

A higher number of NREM S2 spindles at the age of 5 years was associated with more prosocial behaviour at the age of 5, 6 and 9 years, as rated by the parents, and with more prosocial behavior and less hyperactivity at the age of 9 years, as rated by teachers. Regarding trajectories of emotional/behavioural development from the age of 5 to 9 years, participants with a higher number of NREM S2 spindles (median-split) at 5 years also presented with more prosocial behavior at the age of 5, 6 and 9 years ($F_{1,16} = 5.60$, $p = 0.03$, $\eta^2 = 0.26$).

Conclusion

Objectively assessed NREM S2 spindles at the age of five years seem to predict dimensions of emotional/behavioural characteristics at the age of six and nine years. A high number of NREM S2 spindles is associated with individual traits of more prosocial behavior and less hyperactivity.

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P120**Examining Dark Triad traits in relation to sleep disturbances, anxiety sensitivity and intolerance of uncertainty in young adults**

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Background

The Dark Triad (DT) describes a set of three closely related personality traits, Machiavellianism, narcissism, and psychopathy. The aim of this study was to examine the associations between DT traits, sleep disturbances, anxiety sensitivity and intolerance of uncertainty.

Method

A total of 341 adults (M = 29 years) completed a series of questionnaires related to the DT traits, sleep disturbances, anxiety sensitivity, and intolerance of uncertainty.

Results

A higher DT total score was associated with increased sleep disturbances, and higher scores for anxiety sensitivity and intolerance of uncertainty. In regression analyses Machiavellianism and psychopathy were predictors of sleep disturbances, anxiety sensitivity, and intolerance of uncertainty.

Conclusions

Results indicate that specific DT traits, namely Machiavellianism and psychopathy, are associated with sleep disturbances, anxiety sensitivity and intolerance of uncertainty in young adults.

P121**Effect of adjuvant sleep hygiene psychoeducation and lorazepam on depression and sleep quality in patients with major depressive disorders – results from a randomized three-arm intervention**

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Background

Sleep disturbances are a common co-occurring disturbance in patients with major depressive disorders (MDD) and accordingly deserve particular attention. In a randomized design, we investigated the effects of three different adjuvant interventions on sleep and depression among patients with MDD: a sleep hygiene program (SHP), lorazepam (LOR) and their combination (SHP-LOR).

Methods

A total of 120 outpatients with diagnosed MDD (mean age: M = 48.25 years; 56.7% females) and treated with a standard SSRI (citalopram at 20-40mg at therapeutic level) were randomly assigned to one of the following three conditions: sleep hygiene program (SHP; n = 40); lorazepam only (LOR; 1mg/d; n = 40); combination of sleep hygiene program and lorazepam (SHP-LOR; 1mg/d; n = 40). At the beginning and at the end of the study eight weeks later patients completed two questionnaires, the Pittsburgh Sleep Quality Index to assess sleep, and the Beck Depression Inventory to assess symptoms of depression.

Results

Sleep disturbances decreased over time and in all groups. No group differences or interactions were observed. Symptoms of depression decreased over time and in all three groups. Reduction in symptoms of depression was greatest in the SHP-LOR group, and lowest in the LOR group.

Conclusion

The pattern of results suggests that all three adjuvant treatments improved symptoms of sleep disturbances and depression, with greater benefits for the combination of a sleep hygiene program and lorazepam for symptoms of depression, but not for sleep. Nevertheless, risks and benefits of benzodiazepine prescriptions should be taken into account.

P122**Levels of mania and cognitive performance two years after ECT in patients with bipolar I disorder – results from a follow-up study**

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Background

There is limited evidence on the long-term outcomes for patients with bipolar I disorder (BP-I-D) and treated with ECT. Therefore, we asked whether mania scores and cognitive performance at the end of ECT treatment (baseline/BL) predicted mania scores, cognitive performance, recurrence, treatment adherence, and mood (depression; hypomania) two years later (follow-up/FU).

Method

38 patients with BP-I-D undergoing ECT at baseline were followed-up two years later. A brief psychiatric and cognitive assessment (Mini-mental state examination; short-term memory verbal test) was performed; patients completed questionnaires covering recurrence, treatment adherence, and mood (depression; hypomania).

Results

High cognitive performance at BL predicted high cognitive performance at FU; low mania scores at BL predicted low mania scores at FU. By FU, cognitive performance had increased and mania scores decreased. Mania scores and cognitive performance at BL did not predict recurrence, or adherence to medication, or mood (depression; hypomania).

Conclusions

The pattern of results suggests that after two years of successful treatment of acute mania with ECT, cognitive impairment, measured by MMS and a short-term memory verbal test, is not impaired and mood symptom recurrence seems to be improved. Mania scores and cognitive performance at the end of ECT treatment predicted neither mood (depression, hypomania), nor recurrence, or adherence to medication two years later.

P123**Repetitive Transcranial Magnetic Stimulation (rTMS) improved symptoms of obsessive compulsive disorders (OCD), but also cognitive performance? – Results from randomized clinical trial with cross-over design and sham-condition**

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Objective

There is some evidence that rTMS is an effective method of treating patients suffering from OCD. Here, we tested the hypothesis that rTMS has a positive impact both on symptom severity and cognitive performance in such patients. Specifically, short-term verbal processing speed and flexibility were assessed.

Method

Ten patients suffering from refractory OCD and treated with standard medication were randomly assigned either to a treatment-first or to a sham-first condition. At baseline, after two and after four weeks, symptom severity (experts' ratings) and cognitive performance (auditory perception; visual perception: short-term memory and processing speed) were assessed. After two weeks, treatment switched to sham condition, and sham condition switched to treatment condition.

Results

Under treatment but not under sham-conditions, symptom severity reduced. Moreover, cognitive performance improved in parallel.

Conclusions

rTMS is a safe and efficient treatment for patients suffering from refractory OCD; symptoms and cognitive performance improved in parallel.

P124**Children and adolescents suffering from inflammatory bowel disease (IBD) compared to healthy controls: Anthropometric dimensions, blood values, psychological functioning, physical activity and subjective and objective sleep**

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Background

Children and adolescents suffering from IBD report impairments in daily activities, social interactions, coping and sleep. However, as regards psychological functioning, data are conflicting, limited information is available on objectively assessed physical activity (PA) and data on subjective and objective sleep are widely missing. The aims of the present study were, to compare anthropometric dimensions, blood values, psychological functioning, PA, and objective and subjective sleep among children and adolescents suffering from IBD compared to healthy controls.

Method

A total of 47 children and adolescents, (6-19 years) participated. Of these, 23 children and adolescents were diagnosed with IBD (mean age: 13.88 years, 44 % females). The IBD group was divided into a "remission-group" (medically well adjusted) (n=14) and an "active disease" group (n=8). The healthy controls (n=24) were age and gender matches. All participants completed self-rating questionnaires covering socio-demographic data, psychological functioning, subjective PA and subjective sleep disturbances. In parallel, anthropometric data, blood values, objective PA, and objective sleep were assessed.

Results

Children and adolescents suffering from IBD in an active state of the disease reported lower psychological functioning, compared to children and adolescents in remission and healthy controls. Likewise, objective measurements showed higher erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) values, hemoglobin values, and leukocyte values, lower average steps per day, and altered objective sleep patterns (less stage 3 sleep, and more awakenings after sleep onset (WASOs). No mean differences were found between children and adolescents with IBD in remission and healthy controls.

Conclusions

The pattern of results suggests that effective medical treatment of IBD in children and adolescents impacts positively both on psychological dimensions and physiological parameters. Counselling and treatment of children and adolescents with IBD should encourage these young patients and their parents to comply with treatment and not to fear and overestimate the burden of disease.

P125**Influence of aerobic exercise training (AET) using exergames on psychological functioning, sleep and physical performance in children and adolescents suffering from Inflammatory Bowel Disease (IBD)**

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Background

Young patients suffering from IBD have been identified with more mental health issues, lack of favorable sleep quality and less engagement in physical activity (PA) as compared to healthy controls. Standard treatment consists of immune modulating pharmaceuticals, though there is growing evidence that aerobic exercise training (AET) might serve as an additional treatment option. The aim of the present study is to investigate potential AET intervention effects on psychological wellbeing, sleep and PA behaviour in patients with IBD.

Method

21 children and adolescents suffering from IBD and their gender- and age-matched healthy controls (n= 23) were assessed. The IBD group was split into a "remission-group" (medically well adjusted) (n=14) and an "active disease group" (n=7). All participants completed an 8 week AET intervention using exergames reaching 60-80% maximal heart rate for 5 days per week. At baseline and after the 8 week intervention, psychological functioning (Kidsscreen-27; Child-S), objective sleep (EEG) and subjective sleep (ISI) and objective and subjective PA (accelerometer, 6MWT and IPAQ) were assessed.

Results

An 8 week AET intervention significantly improved exercise capacity of all participants, while self-reported fitness and daily PA behavior significantly increased among IBD with active disease. Furthermore, increased disease activity was associated with lower psychological functioning and decreased sleep quality; which could not be abrogated by the intervention.

Conclusions

An AET exergame intervention for eight consecutive weeks, five times a week impacted positively on the exercise capacity in all three groups. Moreover IBD with active disease improved in their fitness and PA behaviour. Future activity interventions should be tested against a non-interventional control group and over a longer time period. However, regular PA seems to be useful in improving many aspects for patients and should be considered as future possible attribution to standard treatment.

P126**The current state of physical activity and exercise programs (PAEPs) in German-Speaking Swiss psychiatric hospitals – results from a brief online survey**

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Background

Physical activity and exercise programs (PAEPs) are an important factor in increasing and maintaining physical and mental health. This holds particularly true for patients suffering from psychiatric disorders and undergoing treatment in a psychiatric hospital. To understand whether the benefits reported in the literature are mirrored in current treatment modalities, the aim of the present study was to assess the current state of PAEPs in psychiatric hospitals in the German-speaking part of Switzerland.

Method

All psychiatric hospitals (N = 55) in the German-speaking part of Switzerland were contacted in spring 2014. Staff responsible for PAEPs was asked to complete an online questionnaire covering questions related to PAEPs such as type, frequency, staff training, treatment rationale, importance of PAEPs within the treatment strategy, and possible avenues to increase PAEPs.

Results

Staff members of 48 different psychiatric hospitals completed the survey. Hospitals provided the following therapeutic treatments: relaxation techniques (100%), sports therapy (97%), activity-related psychotherapeutic interventions (95%), physiotherapy (85%), body therapies (59%), far-eastern techniques (57%) and hippotherapy (22%). Frequencies ranged from once/week to five times/week. About 25% of patients participated in the PAEPs. Interventions were offered irrespective of psychiatric disorders. PAEP-providers wanted and needed more vocational training.

Conclusions

All participating psychiatric hospitals offer a broad variety of PAEPs in their treatment curricula. However, the majority of inpatients do not participate in PAEPs. Furthermore, those who do participate cannot continue to do so following discharge. PAEP-providers need specific extended vocational trainings, and believe that the potential of PA should be improved.

P127**“I love you for ever (more or less)” – Stability and change in adolescents’ romantic love status and associations with mood states**

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Background

Experiencing romantic love is an important part of individual development. Here, we investigated stability and change in romantic love and psychological correlates including mood states, anxiety, and sleep, among Iranian adolescents over a period of eight months.

Method

201 adolescents from an earlier study were contacted eight months later; 157 agreed to participate again. Participants completed a questionnaire covering socio-demographic data, current state of love and mood, including symptoms of depression, anxiety (state, trait), and hypomania. They also completed a sleep and activity log.

Results

Of 64 participants formerly in love, 45 were still in love; of 86 participants not in love at baseline, 69 were still not in love; overall stability was 76%. 17 had fallen in love recently while 19 were no longer in love. Experiencing romantic love was associated with higher anxiety scores. Hypomania scores increased in those newly in love, and decreased in those in a longer-lasting romantic relationship. Sleep and sleep-related variables were not associated with romantic love status.

Conclusion

The pattern of results suggests that among Iranian adolescents the state of love is fairly stable, and that love status seems to be associated with specific states of mood and anxiety.

P128**Exercising impacts on fatigue, depression, and paresthesia in female patients with MS**

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Purpose

Multiple Sclerosis (MS) is a chronic progressive autoimmune disease impacting both body and mind. Typically, patients with MS report fatigue, depression and paresthesia. Standard treatment consists of immune modulatory medication, though there is growing evidence that exercising programs have a positive influence on fatigue and psychological symptoms such as depression. We tested the hypothesis that, as in addition to the standard immune regulatory medication, either yoga or aquatic exercise can ameliorate both fatigue and depression, and we examined whether these interventions also influence paresthesia compared to a non-exercise control condition.

Methods

Fifty-four women with MS (mean age: $M=33.94$ years, $SD=6.92$) were randomly assigned to one of the following conditions: yoga; aquatic exercise; non-exercise control. Their existing immune modulatory therapy remained unchanged. Participants completed questionnaires covering symptoms of fatigue, depression, and paresthesia, both at baseline and on completion of the study eight weeks later.

Results

Compared to the non-exercise control condition and over time, fatigue, depression, and paresthesia decreased significantly in the yoga and aquatic exercise groups. On study completion, the likelihood of reporting moderate to severe depression was 35-fold higher in the non-exercise control condition than in the intervention conditions (yoga and aquatic exercising values collapsed).

Limitations

Only females with MS were enrolled in the study.

Conclusion

The pattern of results suggests that for females with MS and treated with standard immune regulatory medication, exercise training programs such as yoga and aquatic exercising positively impacts on core symptoms of MS, namely fatigue, depression, and paresthesia. Exercise training programs should be considered in the future as possible complements to standard treatments.

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