



Conference Report

# Abstracts of the 5th SFCNS Congress—Swiss Federation of Clinical Neuro-Societies Basel, Switzerland, September 28–30, 2022

## Swiss Federation of Clinical Neuro-Societies

General Office of the Swiss Federation of Clinical Neuro-Societies SFCNS, c/o, IMK Institute for Medicine and Communication Ltd., Münsterberg 1, CH-4001 Basel, Switzerland

**Abstract:** On behalf of the SFCNS, Swiss Federation of Clinical Neuro-Societies, we are pleased to present the abstracts of the 5th SFCNS Congress, which is held in Basel, Switzerland, September 28–30, 2022. In total, 169 abstracts were selected for an ePoster, of which 55 were presented as short presentations during the ePoster Sessions and 5 were presented at the YouClin Research Award Session. We congratulate all the presenters on their research work and contribution.

**Keywords:** neurosurgery; neurology; stroke; neuroradiology; biological psychiatry; epilepsy; neuropsychology; behavioral neurology; clinical neurophysiology; headache; neuropathology; neurorehabilitation

**Citation:** Swiss Federation of Clinical Neuro-Societies. Abstracts of the 5th SFCNS Congress—Swiss Federation of Clinical Neuro-Societies Basel, Switzerland, September 28–30, 2022. *Clin. Transl. Neurosci.* **2022**, *6*, 22. <https://doi.org/10.3390/ctn6030022>

Academic Editor: Claudio Bassett

Received: 15 August 2022

Accepted: 26 August 2022

Published: 8 September 2022

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



**Copyright:** © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

### P001

#### Optical Coherence Tomography Is Associated with Cognitive and Physical Disability in Multiple Sclerosis Independently of Other Biomarkers

N. Cerdá Fuertes <sup>1</sup>, M. Stoessel <sup>1</sup>, A. Cagol <sup>2</sup>, S. Pless <sup>3</sup>, M. Barakovic <sup>2</sup>, P. Calabrese <sup>4</sup>, A. M. Maceski <sup>3</sup>, P. Benkert <sup>5</sup>, K. Gugleta <sup>6</sup>, T. Derfuss <sup>1</sup>, T. Sprenger <sup>7</sup>, C. Granziera <sup>2</sup>, Y. Naegelin <sup>1</sup>, L. Kappos <sup>3</sup>, J. Kuhle <sup>1</sup> and A. Papadopoulou <sup>1</sup>

<sup>1</sup> Neurologic Clinic and Policlinic, Switzerland, Departments of Medicine, Clinical Research and Biomedical Engineering, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>2</sup> Translational Imaging in Neurology (ThINK) Basel, Department of Medicine and Biomedical Engineering, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>3</sup> Research Center for Clinical Neuroimmunology and Neuroscience, University of Basel, Basel, Switzerland

<sup>4</sup> Faculty of Psychology and interdisciplinary Platform Psychology and Psychiatry, Division of Molecular and Cognitive Neuroscience, University of Basel, Basel, Switzerland

<sup>5</sup> Clinical Trial Unit, Department of clinical research, University of Basel, Basel, Switzerland

<sup>6</sup> University Eye Clinic Basel, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>7</sup> DKD Helios Klinik Wiesbaden, Department of Neurology, Wiesbaden, Germany

**Aims:** We aimed at evaluating the relative role of Optical coherence tomography (OCT) next to serum neurofilament light chain (sNfL) and magnetic resonance imaging (MRI), for assessing cognitive and physical disability in multiple sclerosis (MS).

**Methods:** Cross-sectional study with 100 MS patients (63 female, age: 50.4 ± 11.5 years (y); disease duration: 18.7 ± 9.8 y; education: 14.1 ± 3.3 y, 80% with relapsing remitting MS) and 52 matched healthy controls (HC; 34 female, age: 51.4 ± 13.7 y; education: 16.0 ± 3.3 y). All subjects underwent an OCT to assess the mean peripapillary retinal nerve fiber layer (pRNFL) thickness, and the volume of the ganglion cell-inner plexiform (GCIPL) and inner nuclear layers (INL). For patients with prior optic neuritis, we included only the non-affected eye and for the rest, we took the average OCT measures of both eyes.

Brief International Cognitive Assessment for Multiple Sclerosis and the Expanded Disability Status Scale (EDSS) were used to quantify cognitive and physical disability. sNfL levels were measured and T2 lesion volume (T2LV) and brain parenchymal fraction (BPF) were assessed on MRI, using GruSEG and FreeSurfer respectively.

**Results:** Compared to HC, patients had lower mean pRNFL thickness ( $p < 0.001$ ) and GCIPL volume ( $p < 0.001$ ), but INL volume did not differ ( $p = 0.093$ ). After correction for age, vision and education, pRNFL thickness was associated with the symbol digit modalities test (SDMT) in patients ( $\beta = 0.2$ ,  $p = 0.030$ ). In a multivariate analysis including sNfL, BPF and T2LV, pRNFL ( $\beta = 0.19$ ,  $p = 0.044$ ) and T2LV ( $\beta = -0.24$ ,  $p = 0.023$ ) were the only predictors that remained associated with the SDMT.

Mean pRNFL thickness and GCIPL volume showed associations with the EDSS ( $\beta = -0.37$ ,  $p < 0.001$  and  $\beta = -0.46$ ,  $p < 0.001$ ). In a multivariate analysis including sNfL, BPF, and T2LV, GCIPL volume was the strongest predictor of the EDSS ( $\beta = -0.32$ ,  $p < 0.001$ ), followed by sNfL ( $\beta = 0.18$ ,  $p = 0.024$ ).

**Conclusions:** OCT measures, as markers of neuroaxonal loss, are associated with cognitive and physical disability in MS patients independently of serum- (sNfL) and MRI- (BPF, T2LV) markers. Furthermore, GCIPL was the strongest predictor of physical disability. With the advantage of being a quick, patient-friendly examination, needing only minimal post-processing, OCT can play a major role in the stratification of MS patients at risk of higher cognitive and physical disability.

P002

### Therapeutic Burst-Suppression for Refractory Status Epilepticus—A Relevant Treatment Goal? A Single-Center 9-Years Cohort Study

U. Fisch <sup>1</sup>, A. Juenger <sup>2</sup>, S. M. Baumann <sup>2</sup>, S. Marsch <sup>2</sup>, S. Ruegg <sup>1</sup> and R. Sutter <sup>2</sup>

<sup>1</sup> Neurologic Clinic and Polyclinic, University Hospital of Basel, University of Basel, Switzerland

<sup>2</sup> Intensive Care Unit, University Hospital Basel, University of Basel, Switzerland

**Aims:** Current guidelines recommend to treat refractory status epilepticus (RSE) with continuous intravenous anesthetic drugs (IVAD) to achieve a electroencephalographic (EEG) burst attenuation/suppression pattern (BS). However, the evidence for the benefit of BS and its appropriate extent and duration is scarce. This study investigated the frequency of therapeutically induced BS and its association with clinical outcome in adult RSE patients receiving IVAD as antiseizure treatment.

**Methods:** Retrospective analysis of all adult patients treated for RSE with continuous IVAD in an intensive care unit of a Swiss academic tertiary medical center between 2011 and 2019. BS was visually assessed during the first two minutes of each one-hour epoch of EEG monitoring. BS with  $\geq 50\%$  suppression percent was defined according to the American Clinical Neurophysiology Society's (ACNS) Standardized Critical Care EEG Terminology 2021, whereas a BS with a suppression percent between 20–49% was defined as incomplete BS. The primary outcome was the frequency of induced EEG burst-suppression during IVAD treatment. Secondary outcomes were the association of clinical courses and outcomes of RSE patients with the presence of BS or incomplete BS. Logistic regression was performed for outcome analysis.

**Results:** Of 526 adult patients with status epilepticus (SE) between 2011 and 2019, 147 RSE patients with IVAD as antiseizure treatment were identified (median 63 years, 44% female). Thereof, 85 (58%) patients had presumed fatal etiology. Among RSE patients with IVAD, 34 (23%) attained BS and 25 (17%) incomplete BS at least at one time point during EEG monitoring. The univariable comparison between patients with and without persistent termination of RSE did not show an association with the presence of BS ( $p = 0.13$ ), incomplete BS ( $p = 0.41$ ) or absence of any BS ( $p = 0.43$ ). Likewise, the univariable comparison between surviving and non-surviving patients did not show any association

with BS ( $p = 0.83$ ), incomplete BS ( $p = 0.47$ ) or absence of BS ( $p = 0.71$ ). In contrast, presumed fatal etiology was significantly associated with absence of RSE termination ( $p = 0.006$ ) and death ( $p = 0.001$ ).

**Conclusions:** Our results underscore the challenges of achieving EEG BS as recommended during IVAD treatment in patients with RSE. Furthermore, in contrast to SE etiology, our analysis did not find evidence that achievement of BS influences persistent RSE termination or survival.

P003

### Receptor Clustering and Pathogenic Complement Activation in Myasthenia Gravis Depend on Synergy between Antibodies with Multiple Subunit Specificities

T. Derfuss, N. Rose <sup>1</sup>, S. Holdermann <sup>1</sup>, Hi Kim <sup>1</sup>, I. Callegari <sup>1</sup>, I. Fruh <sup>2</sup>, M. Müller <sup>2</sup> and N. Sanderson <sup>1</sup>

<sup>1</sup> University Hospital Basel, Switzerland

<sup>2</sup> Novartis, Basel, Switzerland

Myasthenia gravis is an autoimmune disorder defined by muscle weakness and fatigability associated with antibodies against proteins of the neuromuscular junction (NMJ). The most common autoantibody target is the acetylcholine receptor (AChR). Three mechanisms have been postulated by which autoantibodies might interfere with neurotransmission: direct blockade of acetylcholine binding to receptor, complement-mediated damage of the postsynaptic membrane, and enhanced internalization of the receptor. It is very likely that more than one of these mechanisms operate in parallel, and therefore dissecting the mechanisms of autoantibody-mediated pathology requires patient-derived, monoclonal antibodies.

Using membrane antigen capture activated cell sorting (MACACS) we isolated AChR-specific B cells from patients with myasthenia gravis, and produced and studied recombinant antibodies. All six cloned AChR-antibodies were hypermutated, but of varying isotypes (IgG1, IgG3, IgG4) and recognizing the four different chains of the AChR. Despite strong binding to the receptor, none of the individual antibodies had a strong influence on neuromuscular signal transmission as measured in an in vitro neuromuscular synapse model. They also did not activate complement or induce myasthenic signs in vivo. However, combinations of antibodies induced strong complement activation in vitro, and severe muscle weakness in a passive transfer myasthenia gravis rat model, associated with NMJ destruction and complement activation in muscle. The strongest complement activation was mediated by combinations of antibodies targeting disparate subunits of the AChR, and such combinations also induced the formation of large clusters of AChR on the surface of live cells in vitro. We propose that this synergy between antibodies of different epitope specificities is a fundamental feature of the disease, that can explain the well-known discrepancy between serum anti-AChR titers and clinical severity. This model also has implications for therapeutic strategies currently under investigation.

P004

### MRI-Based Small Vessel Disease Classification of Intracerebral Haemorrhage

M. Goeldlin <sup>1</sup>, M. Mueller <sup>1</sup>, B. Siepen <sup>1</sup>, W. Valenzuela Pinilla <sup>1</sup>, P. Radojewski <sup>1</sup>, A. Hakim <sup>1</sup>, J. Kaesmacher <sup>1</sup>, T. Meinl <sup>1</sup>, L. Clénin <sup>1</sup>, M. Branca <sup>2</sup>, D. Strambo <sup>3</sup>, T. Fischer <sup>4</sup>, F. Medlin <sup>5</sup>, N. Peters <sup>6</sup>, E. Carrera <sup>7</sup>, K. Lövblad <sup>8</sup>, G. Karwacki <sup>9</sup>, C. Cereda <sup>10</sup>, J. Niederhaeuser <sup>11</sup>, M. Mono <sup>12</sup>, A. Mueller <sup>13</sup>, S. Wegener <sup>14</sup>, S. Sartoretti-Schefer <sup>15</sup>, AA. Polymeris <sup>16</sup>, V. Altersberger <sup>16</sup>, M. Psychogios <sup>16</sup>, R. Sturzenegger <sup>17</sup>, M. Schaerer <sup>18</sup>, S.

**Renaud**<sup>19</sup>, **W. Z'Graggen**<sup>1</sup>, **D. Bervini**<sup>1</sup>, **L. Bonati**<sup>20</sup>, **M. Arnold**<sup>1</sup>, **U. Fischer**<sup>21</sup>, **D. Werring**<sup>22</sup> and **D. Seiffge**<sup>1</sup>

<sup>1</sup> Inselspital, Bern University Hospital and University of Bern, Switzerland

<sup>2</sup> Clinical Trials Unit CTU, University of Bern, Switzerland

<sup>3</sup> Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland

<sup>4</sup> Cantonal Hospital St. Gallen, St. Gallen, Switzerland

<sup>5</sup> Cantonal Hospital Fribourg, Switzerland

<sup>6</sup> Klinik Hirslanden Zürich, Switzerland

<sup>7</sup> Geneva University Hospitals (HUG) and University of Geneva (Unige), Switzerland

<sup>8</sup> University Hospital of Geneva, Switzerland

<sup>9</sup> Cantonal Hospital Lucerne, Switzerland

<sup>10</sup> Stroke Center EOC, Neurocenter of Southern Switzerland

<sup>11</sup> Stroke unit, GHOL, Hôpital de zone de Nyon, Switzerland

<sup>12</sup> Stadtspitäler Triemli und Waid, Zurich, Switzerland

<sup>13</sup> University Hospital and University of Zurich, Switzerland

<sup>14</sup> University Hospital Zurich and University of Zurich, Switzerland

<sup>15</sup> Cantonal Hospital Winterthur, Switzerland

<sup>16</sup> University Hospital Basel and University of Basel, Switzerland

<sup>17</sup> Cantonal Hospital of Grisons, Chur, Switzerland

<sup>18</sup> Bürgerspital Solothurn, Switzerland

<sup>19</sup> Réseau Hospitalier Neuchâtelois (RHNe) Pourtalès, Switzerland

<sup>20</sup> Reha Rheinfelden and University of Basel, Switzerland

<sup>21</sup> University Hospital Basel and Inselspital, Bern University Hospital, Switzerland

<sup>22</sup> University College London (UCL), UK

**Background:** Cerebral small vessel disease (SVD) is the major cause of intracerebral hemorrhage (ICH), but there is no comprehensive classification of ICH subtypes according to different SVD phenotypes. We aimed to develop an MRI-based classification for SVD-related ICH and assess association with outcomes.

**Methods:** We performed a retrospective study of prospectively collected data of patients enrolled in the national, multicenter Swiss Stroke Registry from 2013–2019. We included consecutive patients with non-traumatic, SVD-related ICH and available MRI. Patients were classified according to a novel MRI-based classification using haemorrhagic (microbleeds, cortical siderosis) and non-haemorrhagic (white matter hyperintensities, lacunes, perivascular spaces) MRI markers and haematoma location as cerebral amyloid angiopathy (CAA), deep perforator arteriopathy (DPA), mixed SVD or undetermined SVD. The primary clinical outcomes were recurrent ICH or ischemic stroke at 3 months. We performed a Firth penalized logistic regression and competing risk analysis according to Fine and Gray.

**Results:** We enrolled 1180 patients (age (IQR) 73 (62–80) years, baseline NIHSS 6 (2–12), 538/1180 (45.6%) lobar hematoma location, systolic blood pressure on admission 166 (145–185) mmHg). During follow-up 57 patients had 58 events (29 ICH, 29 ischemic strokes, event rate 4.8%). The rate of recurrent ICH and ischaemic stroke at 3 months was 4%/1% for CAA, 0.7%/2.6% for DPA, 2.7%/2.9% for mixed SVD and 3.8%/3.4% for undetermined SVD, respectively, without a statistically significant difference between groups. Discussion: This new MRI-based SVD-ICH phenotype classification based on objective radiological markers is feasible and may improve classification and reporting of ICH subtypes in clinical practice and research.

P005

**Omicron Breakthrough Disease Activity in the Swiss Multiple Sclerosis Cohort Study**

**V. Eppel**<sup>1</sup>, **L. Demuth**<sup>1</sup>, **L. Develioglou**<sup>1</sup>, **A. Orleth**<sup>1</sup>, **S. Subramaniam**<sup>2</sup>, **S. Schädelin**<sup>2</sup>, **P. Benkert**<sup>2</sup>, **A. Frentzel**<sup>1</sup>, **M. Käch**<sup>1</sup>, **D. Jorganxhi**<sup>1</sup>, **N. Sanderson**<sup>1</sup>, **K. Ivanek**<sup>1</sup>, **L. Kappos**<sup>3</sup>, **J. Oechtering**<sup>1</sup>, **L. Achtnichts**<sup>4</sup>, **J. Saxer**<sup>4</sup>, **C. Pot**<sup>5</sup>, **P. Lim Dubois-Ferriere**<sup>5</sup>, **P. Lalive**<sup>6</sup>, **G. Breville**<sup>6</sup>, **C. Bridel**<sup>6</sup>, **C. Gobbi**<sup>7</sup>, **C. Zecca**<sup>7</sup>, **G. Disanto**<sup>7</sup>, **S. Müller**<sup>8</sup>, **F.**

Grünenfelder <sup>8</sup>, A. Salmen <sup>9</sup>, T. Derfuss <sup>1</sup>, C. Berger <sup>1</sup>, R. Pedotti <sup>10</sup>, C. Raposo <sup>10</sup>, K. Leuzinger <sup>1</sup>, H. Hirsch <sup>1</sup>, C. Granziera <sup>1</sup>, J. Kuhle <sup>1</sup> and M. Mehling <sup>1</sup>

<sup>1</sup> Universitätsspital Basel und Universität Basel, Switzerland

<sup>2</sup> Universitätsspital Basel, Switzerland

<sup>3</sup> Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB) Basel, Universitätsspital Basel und Universität Basel, Switzerland

<sup>4</sup> Kantonsspital Aarau, Switzerland

<sup>5</sup> Centre Hospitalier Universitaire Vaudois (CHUV) et Université de Lausanne, Switzerland

<sup>6</sup> Hôpitaux Universitaires de Genève (HUG) et Université de Genève, Switzerland

<sup>7</sup> Ente Ospedaliero Cantonale (EOC) e l'Università della Svizzera italiana (USI), Switzerland

<sup>8</sup> Kantonsspital St. Gallen, Switzerland

<sup>9</sup> Inselspital Bern, Switzerland

<sup>10</sup> F. Hoffmann-La Roche Ltd., Switzerland

**Introduction:** In patients with Multiple Sclerosis (pwMS), specific disease modifying treatments (DMTs) may compromise immune response following SARS-CoV-2 vaccination. Limited information is available, whether levels of anti-SARS-CoV-2 antibodies are linked to the risk of breakthrough infections in pwMS.

**Aims:** To determine the rate of Omicron breakthrough infection and severity of COVID-19 in a cohort of MS patients treated with different DMTs and to estimate the impact of SARS-CoV-2-specific antibody levels on breakthrough infection risk.

**Methods:** This study is nested within the Swiss MS Cohort, a nationwide multicenter study that has recruited 1585 pwMS. Patients who received two doses of SARS-CoV-2 vaccines before Omicron became the dominant variant in Switzerland on 15 December 2021 and had a follow-up thereafter were included. Data on SARS-CoV-2 infections, severity of COVID-19 according to the WHO scale and SARS-CoV-2 vaccines were collected by questionnaires. Anti-SARS-CoV-2-S antibody levels were measured after the second vaccine dose. Incidence of infections grouped by antibody level after second vaccination was visualized using Kaplan-Meier curves. Cox regression models were used to estimate the impact of antibody levels on the hazard of breakthrough infection during follow-up.

**Results:** 242 pwMS (median age 49 years, 162 (67%) female, 36 (15%) with progressive disease, median EDSS 2.5) were included. 22 (9%) had SARS-CoV-2 infection and 137 (57%) at least one additional vaccine dose prior to Omicron start. Since then, 57 breakthrough infections were reported. Severity of breakthrough disease on WHO scale ranged from 1–10. 7 were asymptomatic, 46 were symptomatic as outpatients, 3 were hospitalized and 1 died. Patients with antibody levels > 150 U/mL (n = 95) after second vaccination had a 64% reduced risk for Omicron breakthrough-infection compared to patients with antibody levels < 0.7 U/mL (n = 81) (HR 0.36, 95% CI = 0.18–0.71, *p* < 0.01). This effect was maintained after adjustment for DMT at vaccination and time since second vaccination.

**Conclusions:** Humoral immune response after second SARS-CoV-2 vaccination is associated with Omicron breakthrough infection rate, a finding contrasting general populations, where antibody levels seem to have little impact on protecting from Omicron infection. Most breakthrough infections in our cohort were mild. Analyses on the effect of booster vaccinations on serology and infection rates will follow.

P006

**The Spinal Cord Lateral Tract Sign as an rAMIRA-Based MRI Sign for Upper Motor Neuron Involvement in Amyotrophic Lateral Sclerosis in a Clinical Setting**

M. J. Wendebourg <sup>1</sup>, L. Sander <sup>1</sup>, E. M. Kesenheimer <sup>1</sup>, M. Weigel <sup>2</sup>, T. Haas <sup>3</sup>, C. Weidensteiner <sup>2</sup>, C. Neuwirth <sup>4</sup>, N. Braun <sup>4</sup>, M. Weber <sup>4</sup>, K. Jahn <sup>5</sup>, C. Granziera <sup>6</sup>, K. Schweikert <sup>7</sup>, M. Sinnreich <sup>7</sup>, O. Bieri <sup>2</sup> and R. Schlaeger <sup>1</sup>

<sup>1</sup> Department of Neurology and Department of Clinical Research, University Hospital Basel, University of Basel, Basel, Switzerland

<sup>2</sup> Division of Radiological Physics, Department of Radiology, University Hospital Basel and Department of Biomedical Engineering, University of Basel, Basel, Switzerland

<sup>3</sup> Division of Radiological Physics, Department of Radiology, University Hospital Basel, Basel, Switzerland

<sup>4</sup> Neuromuscular Diseases Unit/ALS Clinic, Kantonsspital, St. Gallen, Switzerland

<sup>5</sup> Clinics of Respiratory Medicine, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>6</sup> Translational Imaging in Neurology (ThINk), Department of Biomedical Engineering, University of Basel, Basel, Switzerland

<sup>7</sup> Department of Neurology, University Hospital Basel, Basel, Switzerland

**Background/Aims:** Signs of upper motor neurons (UMN) dysfunction can be elusive and difficult to identify in amyotrophic lateral sclerosis (ALS) (1), but are important for timely diagnosis (2). One of the core macro-pathological features of ALS, the spinal cord lateral tract (SCLT) sclerosis, was described by Charcot and shaped the name of the disease (3). Histopathologically, these areas are characterized by axonal loss and diffuse astrocytic gliosis (4, 5). Averaged Magnetization Inversion Recovery Acquisitions (rAMIRA) is a novel MRI approach enabling spinal cord (SC) gray and white matter (WM) imaging with high contrast in clinically feasible acquisition times at 3 Tesla (T) (6, 7). The aims of the study were to define and validate the SCLT sign and to investigate its sensitivity and specificity in patients with ALS, other lower-motor neuron (LMN) diseases, and healthy controls (HC).

**Methods:** 38 patients with an established diagnosis of ALS (Gold Coast criteria), 60 HC, 25 patients with post-polio syndrome (PPS, March of Dimes criteria), and 10 patients with 5q-spinal muscular atrophy (SMA) were investigated by axial 2D rAMIRA imaging at the intervertebral disc levels C2/C3–C5/C6 (3T-PRISMA, Siemens). Clinical and demographic data of all participants were obtained. The SCLT sign was defined and validated in a multi-step process by 4 independent raters in subsets of participants and its sensitivity and specificity in detecting ALS were calculated.

**Results:** The SCLT sign, defined as evenly spread, uni- or bilateral hyperintensities in the SC WM dorsolaterally to the anterior horns, was present in ALS patients in 50%, 49%, 54% and 46% at the respective levels C2/C3–C5/C6, and in up to 89% of ALS patients with UMN predominance. In the HC, PPS and SMA groups, the sign was present in 3%, 8%, and 0%, respectively, thus rendering a sensitivity of 58% and specificity of 98% at C3/C4 to identify ALS cases. The sign was detectable irrespective of disease duration and persisted on serial imaging over 2 years.

**Conclusions:** The SCLT sign shows a high specificity in distinguishing patients with ALS from HC and patients with other LMN disorders. Further investigations of patients early in the disease course, particularly those without clinical signs of UMN dysfunction, and of patients with other UMN disorders are necessary next steps to estimate the potential of this novel imaging marker to improve the ALS diagnostic process.

P007

## Atrophy of the Cervical Spinal Cord Gray Matter: a New Surrogate Marker in Amyotrophic Lateral Sclerosis

E. M. Kesenheimer <sup>1</sup>, M.J. Wendebourg <sup>1</sup>, M. Weigel <sup>2</sup>, N. Naumann <sup>1</sup>, K. Jahn <sup>3</sup>, T. Haas <sup>2</sup>, L. Sander <sup>1</sup>, N. Braun <sup>4</sup>, C. Neuwirth <sup>4</sup>, C. Granziera <sup>5</sup>, M. Weber <sup>4</sup>, K. Schweikert <sup>1</sup>, M. Sinnreich <sup>1</sup>, O. Bieri <sup>2</sup> and R. Schläger <sup>1</sup>

<sup>1</sup> Department of Neurology and Department of Clinical Research, University Hospital Basel, University of Basel, Basel, Switzerland

<sup>2</sup> Division of Radiological Physics, Department of Radiology, University Hospital Basel, Basel, Switzerland

<sup>3</sup> Clinics of Respiratory Medicine, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>4</sup> Neuromuscular Diseases Unit/ALS Clinic, Kantonsspital St. Gallen, St. Gallen, Switzerland

<sup>5</sup> Translational Imaging in Neurology (ThINk), Department of Biomedical Engineering, University of Basel, Basel, Switzerland

**Background:** There is an urgent need for valid and reliable imaging biomarkers to reduce the diagnostic delay, to monitor the disease course, and to evaluate drug efficacy in upcoming trials in amyotrophic lateral sclerosis (ALS). The novel AMIRA (Averaged Magnetization Inversion Recovery Acquisitions) method enables high resolution MR-imaging with improved contrast of spinal cord (SC) gray matter (GM) and white matter in clinically feasible acquisition times at 3 Tesla. (1,2).

**Aims:** The aims of this study were to compare cervical SC GM areas between patients with a diagnosis of ALS and healthy, age- and sex-matched control subjects (HC) and to assess the association of cervical SC GM area and established measures of clinical disability, the revised ALS functional rating scale and of respiratory impairment, the sniff nasal inspiratory pressure (SNIP) in ALS.

**Methods:** Using axial 2D radial (r)AMIRA imaging(1) at the cervical intervertebral disc level C3/C4 acquired at a 3T PRISMA scanner (Siemens healthineers) and a semi-automated segmentation approach (JIM7, www.xinapse.com), we compared SC GM areas of 36 patients diagnosed with ALS according to the Gold Coast criteria(3) (mean age 61.7 yrs, 14 women, with bulbar and spinal onset, mean disease duration 32.9 months) and 36 age- and sex-matched HC. The associations between SC GM area and disability metrics (ALSFRS-R(4) and SNIP(5)) were assessed by multivariable regression analyses with adjustment for age and sex.

**Results:** SC GM area at the level C3/C4 was significantly reduced in patients with ALS compared to HC (mean GM area in mm<sup>2</sup> (SD): ALS 16.6 (2.3); HC 19.65 (2.7); relative reduction 15.4%,  $p < 0.0001$ ). In multivariable regression analyses adjusting for age and sex, GM area at C3/C4 explained 36.1% of ALSFRS-R variance ( $p = 0.0001$ ) and 32.2% of SNIP variance in patients with ALS, respectively.

**Conclusions:** Cervical SC GM area in ALS patients shows significant atrophy compared to HC and correlates with established measures of clinical disability and respiratory impairment, namely ALSFRS-R and SNIP. Further longitudinal investigations, particularly of patients early in the disease course, are necessary next steps to evaluate the potential of this novel and easy to assess imaging marker for monitoring and predicting the disease course, and its potential as a surrogate in upcoming drug trials.

P008

## Herpes Zoster Burden of Disease: An Analysis of The Placebo Group Data from Three Randomized Phase III Studies

D. Curran <sup>1</sup>, S. Matthews <sup>2</sup>, C. Boutry <sup>1</sup>, N. Lecrenier <sup>1</sup>, A. L. Cunningham <sup>3</sup> and K. Schmader <sup>4</sup>

<sup>1</sup> GlaxoSmithKline, Belgium

<sup>2</sup> Freelance c/o GlaxoSmithKline, Belgium

<sup>3</sup> The Westmead Institute for Medical Research, Australia

<sup>4</sup> Duke University Medical Center and Durham VA Health Care System, USA

**Aims:** The risk of herpes zoster (HZ) is associated with a decline in the immune system function, linked to aging and/or in individuals who are immunocompromised or immunosuppressed due to disease or therapy. In this post-hoc analysis, we describe the incidence and burden of HZ pain in immunocompetent patients  $\geq 50$  years of age (YOA) and in hematopoietic stem cell transplantation (HSCT) recipients aged  $\geq 18$  YOA.

**Methods:** ZOE-50 (NCT01165177), ZOE-70 (NCT01165229) and ZOE-HSCT (NCT01610414) were phase III, observer-blind, placebo-controlled, randomized studies conducted in immunocompetent adults  $\geq 50$  YOA (ZOE-50) and  $\geq 70$  YOA (ZOE-70); and in HSCT recipients aged  $\geq 18$  YOA, respectively. Studies were conducted between August 2010 and July 2015, and between July 2012 and February 2017 for the ZOE-50/ZOE-70 and ZOE-HSCT studies, respectively. The participants received 1 or 2 doses of the adjuvanted recombinant zoster vaccine or placebo, 1 to 2 months apart. The analysis was performed

on unvaccinated/placebo subjects who had a confirmed HZ episode during the original studies. HZ pain and interference with activities of daily living was assessed by the Zoster Brief Pain Inventory instrument.

**Results:** Overall, 280 HZ confirmed patients aged  $\geq 50$  YOA, 240 HZ patients aged  $\geq 70$  YOA, and 172 HZ patients aged  $\geq 18$  YOA were included in the placebo groups for the ZOE-50, ZOE-70 and ZOE-HSCT studies, respectively. The incidence of HZ was 9.1/1000 person years in both the ZOE-50 and ZOE-70 placebo groups and 95.6/1000 person years in the ZOE-HSCT study placebo group. In the 3 studies, the majority of individuals with HZ experienced severe pain, with approximately 90% of individuals reporting clinically significant pain. Descriptive statistics on the location of the rash, number of dermatomes involved, the presence of pain and pain intensity will be presented by study group.

**Conclusions:** Our assessments show that the incidence and burden of HZ is high in immunocompetent adults aged  $\geq 50$  YOA and even more so in HSCT recipients aged  $\geq 18$  YOA.

P009

### Long-Term Blood Pressure Variability is Associated with White Matter Integrity and Cognitive Decline in Patients with Mild Cognitive Symptoms and Cerebral Amyloid Angiopathy

L. Sveikata<sup>1</sup>, M. C. Zanon Zotin<sup>2</sup>, D. Schoemaker<sup>2</sup>, A. Chokesuwattanaskul<sup>2</sup>, V. Perosa<sup>2</sup>, M. Etherton<sup>2</sup>, Y. Ma<sup>3</sup>, A. Charidimou<sup>2</sup>, A. Biffi<sup>2</sup>, E. M. Gurol<sup>2</sup>, S. M. Greenberg<sup>2</sup> and A. Viswanathan<sup>2</sup>

<sup>1</sup> Geneva University Hospitals (HUG), Switzerland; Massachusetts General Hospital and Harvard Medical School, Boston, USA

<sup>2</sup> Massachusetts General Hospital and Harvard Medical School, Boston, USA

<sup>3</sup> Harvard T.H. Chan School of Public Health, USA

**Background:** Emerging evidence suggests that long-term blood pressure variability (BPV) may contribute to cerebral small vessel disease progression and cognitive impairment beyond the deleterious effects of elevated blood pressure. (1,2) We investigated whether BPV is associated with white matter (WM) microstructural integrity and cognitive decline in elderly individuals with cerebral amyloid angiopathy (CAA), a well-characterized cerebral small vessel disease.

**Methods:** We recruited 131 non-demented individuals ( $73.3 \pm 7.0$  y, 33/101 female/male, MMSE  $27.5 \pm 2.0$ ) from the Massachusetts General Hospital memory-clinic cohort with and without CAA (24/50 possible/probable CAA) according to modified Boston criteria. Participants underwent detailed neuropsychological testing and a 3 T research MRI. Visit-to-visit BPV was assessed using the coefficient of variation derived from serial BP measures during a 5-year interval. A novel diffusion tensor imaging marker—peak width of skeletonized mean diffusivity (PSMD)—was used to evaluate the WM integrity. (3) We used linear regression models to assess the association between BPV with PSMD and domain-specific cognitive decline. Models were adjusted for mean BP, age, sex, hypertension, antihypertensive medication, diabetes, smoking, and body mass index.

**Results:** We found a strong association between loss of WM integrity and high systolic BPV ( $\beta = 0.43$ ,  $p < 0.001$ ). The association remained significant in the adjusted regression model ( $\beta = 0.41$ ,  $p < 0.001$ ). Furthermore, the association of BPV with WM integrity was stronger when CAA was present ( $\beta = 9.33$ ,  $P$  for interaction  $< 0.023$ ). Higher BPV was associated with decline in global cognition ( $\beta = -0.24$ ,  $p = 0.035$ ) and processing speed ( $\beta = -0.30$ ,  $p = 0.022$ ). BPV also had a weak association with decline in executive function ( $\beta = -0.19$ ,  $p = 0.106$ ), and memory ( $\beta = -0.19$ ,  $p = 0.095$ ).

**Conclusions:** Our findings show that long-term BPV is associated with microstructural vascular white matter injury that may contribute to domain-specific cognitive decline in older adults. The association between BPV and white matter integrity may in part be



driven by CAA-related vascular dysfunction. Better control of BPV could be a novel therapeutic target to slow cognitive decline over time. As a next step, we will use BP telemonitoring technologies to evaluate whether real-world BP fluctuations contribute to vascular brain injury and vascular cognitive impairment.

P010

### Neurostatus-SMARTCARE in Comparison to Standard Neurostatus-EDSS®—A Prospective Swiss Multicenter Randomized Cross-Over Study

G. Mallucci <sup>1</sup>, A. Zimmer <sup>1</sup>, N. Sfikas <sup>2</sup>, A. Ocampo <sup>2</sup>, B. Kieseier <sup>2</sup>, A. Khanna <sup>2</sup>, L. Kappos <sup>1</sup> and M. D'Souza <sup>3</sup>

<sup>1</sup> Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), Departments of Head, Spine and Neuromedicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital and University of Basel, Switzerland <sup>2</sup> Novartis Pharma AG, Switzerland

<sup>3</sup> Neurologic Clinic and Polyclinic, Department of Head, Spine and Neuromedicine, University Hospital of Basel, Switzerland

**Background:** Multiple sclerosis (MS) is a chronic neurological disease and patients present with symptoms, which can occur as relapses or as progressive neurological deterioration. Comprehensive, standardized clinical neurological assessment is the gold standard to evaluate activity and to track disability over time. The Neurostatus-eEDSS® is the standard assessment deployed in MS randomized clinical trials (RCT), typically serving as the primary endpoint. COVID-19 pandemic has impacted conduct clinical studies. This opened opportunities to adapt the data capture systems in clinical trials i.e., conducting neurological assessments on phone or video. We have developed a new version of Neurostatus-eEDSS® for trained non-neurologist healthcare professionals (HCP) to perform these assessments. This Neurostatus-SMARTCARE (“smartly modernized assessment: recorded, telemedical, care professional-assisted, remotely evaluated”) assessment is video recorded, allowing neurologists to review and re-assess the ratings for quality control as needed.

**Aim:** to assess the concordance between Neurostatus-SMARTCARE, performed by HCPs, and Neurostatus-EDSS®, performed by neurologists.

**Methods:** A multicentre randomized cross-over study in Switzerland with 100 MS patients that have consented to participate are randomized 1:1 to group A or group B. Group A undergoes first Neurostatus-EDSS® and afterwards Neurostatus-SMARTCARE—group B starts with Neurostatus-SMARTCARE and finishes with Neurostatus-EDSS®. At the next regular visit –i.e., 6 or 12 months- the reverse order is applied. The HCP and neurologist performing the evaluations are blinded to each others findings and assessment scores. All examinations are entered into an electronic case report form and video recorded.

**Conclusions:** The combination of a video recorded system and an expert assessment presents a unique opportunity for innovation in MS RCTs. In addition, Neurostatus-SMARTCARE may be extended to clinical care settings by allowing home based assessment by MS HCPs, thereby reducing the burden on patients and caregivers. Furthermore it offers the potential for more frequent remote assessments and reducing the costs.

P011

### Brain Fog in Neuropathic Postural Tachycardia Syndrome: Associated with Autonomic Hyperarousal?

B. Rodriguez <sup>1</sup>, A. Hochstrasser <sup>1</sup>, P. Eugster <sup>2</sup>, E. Grouzmann <sup>2</sup>, R. M. Müri <sup>1</sup> and W. J. Z'Graggen <sup>1</sup>

<sup>1</sup> Inselspital—Universitätsspital Bern, Switzerland

<sup>2</sup> CHUV—University Hospital, Switzerland

**Background:** Brain fog is a common and highly disturbing symptom for patients with neuropathic postural tachycardia syndrome (POTS). Cognitive deficits have been measured exclusively in the upright body position and mainly comprised impairments of higher cognitive functions. The cause of brain fog is still unclear today. This study aimed to investigate whether increased autonomic activation might be an underlying mechanism for the occurrence of brain fog in neuropathic POTS. We therefore investigated cognitive function in patients with neuropathic POTS and a healthy control group depending on body position and in relation to norepinephrine release as a sensitive indicator of acute stress. The second aim was to test the effect of water intake on cardiovascular regulation, orthostatic symptoms, cognitive function and norepinephrine release.

**Methods:** Thirteen patients with neuropathic POTS and 15 healthy control subjects were included. All participants completed a total of four rounds of cognitive testing: two before and two after the intake of 500 mL still water, each first in the supine position and then during head-up tilt. At the end of each cognitive test, a blood sample was collected for determination of plasma norepinephrine. After each head-up tilt phase participants were asked to rate their current symptoms on a visual analogue scale.

**Results:** Working memory performance in the upright body position was impaired in patients, which was associated with self-reported symptom severity. Patients had elevated plasma norepinephrine independent of body position and water intake that increased excessively in the upright body position. The excessive increase of plasma norepinephrine was related to heart rate and symptom severity. Water intake in patients decreased norepinephrine levels and heart rate, and improved symptoms as well as cognitive performance.

**Conclusions:** Brain fog and symptom severity in neuropathic POTS are paralleled by an excessive norepinephrine secretion. Bolus water drinking down regulates norepinephrine secretion and improves general symptom severity including brain fog.

P012

### Frequency Dependent Interindividual Variability of the Deep Brain Stimulation Effect on Upper-Limb Bradykinesia

P. Dorin, D. Brogle, S. Hägele-Link, M. Krüger, G. Kägi and F. Brugger

Kantonsspital St. Gallen, Switzerland

**Objective:** To demonstrate that there are interindividual differences in the response of upper limb bradykinesia to subthalamic deep brain stimulation (STN-DBS) in patients with Parkinson's disease (PD) depending on the stimulation frequency used.

**Background:** There is evidence that increasing stimulation frequency of STN-DBS beyond the standard settings of 130 Hz may improve tremor, whereas lower frequencies "<100 Hz" are more beneficial for axial motor symptoms. There are also indications that the improvement of upper limb motor symptoms varies between patients depending on the frequency used.

**Methods:** A kinematic analysis of a finger-tapping train for 20 sec. was assessed in 13 PD patients (median: 63 years; range 56–71 years) with chronic (">3" months) bilateral STN-DBS after overnight PD drug withdrawal. Frequencies were varied in intervals of 10 Hz from 60–180 Hz (randomized sequence), while the TEED was kept stable. Every train of finger-tapping was performed twice for each frequency five minutes after the frequency had been changed. The decrement of the amplitude of the finger taps (i.e., distance between index finger and thumb) was measured by means of a kinematic system and

estimated by fitting a regression line to the amplitude values. The regression coefficients were compared statistically.

**Results:** As expected the amplitude decrement of finger taps improved under DBS compared to the state off DBS (" $p < 0.001$ "). The optimal stimulation frequency with the least decrement varied from patient to patient. There was no consistent peak frequency across patients. Similar observations were made for the worst stimulation frequencies which in a few patients resulted in an even worse motor performance than off DBS.

**Conclusions:** Our results indicate that the effect of DBS on upper limb bradykinesia varies across individuals depending on the frequency used. The standard frequency of 130 Hz may not yield the best motor response to DBS in all individuals. We propose that evaluating different stimulation frequencies may contribute to an optimisation of the DBS effect, whereas the concept of "one frequency fits all" should be abolished.

P013

### Evaluation of the Surgical Versus Endovascular Treatment of Ruptured and Unruptured Pericallosal Aneurysms: An International Multicentric Study

J. Haemmerli <sup>1</sup>, A. Bervitskiy <sup>2</sup>, E. Kurz <sup>3</sup>, J. Turpin <sup>4</sup>, A. Dehdashti <sup>4</sup>, F. Ringel <sup>3</sup>, J. Rzaev <sup>2</sup>, K. Schaller <sup>5</sup> and P. Bijlenga <sup>5</sup>

<sup>1</sup> Hôpitaux universitaires de Genève, Switzerland

<sup>2</sup> The "Federal Centre of Neurosurgery" of the Ministry of health of the Russian Federation Novosibirsk, Russia

<sup>3</sup> University Medical Center Mainz, Germany

<sup>4</sup> Donald and Barbara Zucker School of Medicine at Hofstra Northwell, USA

<sup>5</sup> Hôpitaux Universitaires de Genève, Switzerland

**Aims:** Treatment of pericallosal aneurysms (PeriAy), whether endovascular or surgical, relies more on the neurovascular team experience than on evidence-based guidelines. This study aims to compare endovascular and surgical treatments of PeriAy, ruptured and unruptured.

**Methods:** All data were extracted from the Pericallosal Aneurysm Study Group data base, an multicentric international cohort collecting data on patients treated for at least one PeriAy, ruptured and unruptured. Outcomes were compared by endovascular versus surgical treatments, and by rupture status. The primary outcome was the mRS at 12 months. Secondary outcomes were the aneurysmal complete occlusion at 12 months, the rate of complications, and vasospasms requiring invasive treatment.

**Results:** One hundred and sixteen treated pericallosal aneurysms were included, 31 (26.7%) were treated endovascularly and 85 (73.3%) were treated surgically. Fifty-three treatments concerned ruptured PeriAy (21 endovascular (67.7%), 32 surgical (37.6%) ( $p < 0.001$ )). Demographics were similar between groups.

No difference regarding the mRS at 12 months was observed between the treatment groups (endovascular and surgical groups respectively (median): all 0 [Q1:0, Q3:2], 0 [Q1:0, Q3:1]; unruptured 0 [Q1:0, Q3:1], 0 [Q1:0, Q3:1]; ruptured 0 [Q1:0, Q3:2], 0 [Q1:0.5, Q3:2]).

No residual perfusion of the PeriAy was observed in the surgical treatment group, whereas 44.4% of the endovascularly-treated aneurysms were found to have residual perfusion ( $p < 0.001$ ). The need of invasive treatment for vasospasm was significantly lower in the surgical group (12.5%) compared to the endovascular group (38.1%,  $p = 0.04$ ). No difference was observed regarding the complication rate (endovascular 29%, surgical 16.5%,  $p = 0.19$ ).

**Conclusions:** Although surgical treatment reduces the risk of aneurysmal residual perfusion and the need of invasive treatment for vasospasms, ruptured PeriAy are more often treated endovascularly. PeriAy should be considered for surgical treatment,

especially if ruptured. Endovascular treatment should be reserved for morbid patients with surgical risk. Multicentric data collection is still ongoing.

P014

### Microglia-Specific Disruption of Sialic Acid-Siglec-9/E Interactions: A Novel Immunotherapy against Glioblastoma?

P. Schmassmann, J. Roux, T. A. Martins, M. Ritz, T. Shekarian, H. Läubli and G. Hutter

University Hospital Basel, Switzerland

**Aims:** Recently, ‘don’t eat me’-signals like CD47 have emerged as novel innate immune checkpoints, enabling cancer cells to evade clearance by phagocytes such as monocyte-derived macrophages (M<sub>DM</sub>) or microglia (MG). Here, we aim at defining the role of inhibitory Siglec-9 in human and its mouse homologue Siglec-E in MG-centered immunotherapy against GBM.

**Methods:** We employed a CT-2A orthotopic GBM mouse model with MG specific (Sall 1-CreERT2 x Siglec-flox) and whole innate-compartment (Cx 3cr 1-CreERT2 x Siglec-flox) spatio-temporal deletion of Siglec. We applied multi-color flow cytometry, transcriptomics and proteomics analysis to decipher the immune response upon Siglec knockout.

**Results:** TCGA RNA-sequencing data revealed a significant correlation between high expression of immunoinhibitory SIGLEC9 and poor survival in GBM patients (log-rank  $p = 0.02$ ). In the MG specific spatio-temporal deletion of Siglec (Sall 1-CreERT2 x Siglec-flox), we observed high MG-proliferation upon Siglec-E knockout (Ki-67+ MG 14.8% in Cre- vs. 34.9% in Cre+,  $p < 0.0001$ ) accompanied by an enhanced microglial GBM-cell uptake (5.6% in Cre- vs. 12.3% in Cre+,  $p < 0.001$ ). By extending the Siglec knockout to the M<sub>DM</sub> compartment in our glioma mouse model (Cx 3cr 1-CreERT2 x Siglec-flox) we observed a significantly prolonged survival in the Cx 3cr 1-Cre+ population (21 d in Cre- vs. 27 d post-tumor injection in Cre+,  $p = 0.018$ ), which could be further promoted by combining Siglec knockout with CD47 blockade (11% long-term remission in Cre+ + anti-CD47). Proteomics analysis revealed increased antigen processing and presentation capabilities of Siglec knockout M<sub>DM</sub>s which was confirmed by ex-vivo OT-1 cross-presentation assays. This increased T cell priming upon M<sub>DM</sub> Siglec knockout was further boosted by addition of anti-PD1 antibody to the Siglec knockout + anti-CD47 combination. Resulting in 23% of animals experiencing long-term remission in the triple treatment arm, even after tumor re-challenge. By genetically targeting sialic acids, the ligand for Siglec receptors, on CT-2A cells (GNE-KO), we observed a strong innate and adaptive immune response with increased GBM-cell phagocytosis by MG and M<sub>DM</sub>s and less exhausted tumor-infiltrating CD8+ T cells (14.8% in WT vs. 5.9% in GNE-KO,  $p = 0.003$ ).

**Conclusions:** These data identify the sialic-acid-Siglec-E pathway as an anti-phagocytic signal in a pre-clinical GBM model, and demonstrate its therapeutic potential in GBM immunotherapy.

P015

### Single-Cell Characterization of Human GBM Reveals Regional Differences in Tumor-Infiltrating Leukocyte Activation

P. Schmassmann<sup>1</sup>, J. Roux<sup>1</sup>, S. Dettling<sup>2</sup>, S. Hogan<sup>1</sup>, T. Shekarina<sup>1</sup>, T. A. Martins<sup>1</sup>, M. Ritz<sup>1</sup>, S. Herter<sup>2</sup>, M. Bacac<sup>2</sup> and G. Hutter<sup>1</sup>

<sup>1</sup> University Hospital Basel, Switzerland

<sup>2</sup> Roche Innovation Center, Switzerland

**Background:** Clinical trials of systemic T cell checkpoint blockade in GBM patients showed only disappointing results. This may be attributed in part to the immunosuppressive components of the GBM immune tumor microenvironment (iTME). Therefore, major efforts have been undertaken to describe the GBM iTME on a single cell level. However, human data on the composition of the iTME in different tumor regions (contrast enhancing tumor center versus peripheral infiltration zone) remain scarce.

**Methods:** Here, we performed high-depth single-cell RNA sequencing (scRNA-seq) on patient-matched biopsies from tumor center and the peripheral infiltration zone of five primary GBM patients. Additionally, peripheral blood mononuclear cells (PBMC) of the same patients were included in the analysis to explore the transcriptional changes occurring during tumor infiltration of circulating immune cells. Main findings of the transcriptional analysis were confirmed by flow cytometry.

**Results:** Through analysis of >45,000 cells, we revealed a distinct regional transcriptional profile of microglia (MG) and monocyte-derived macrophages (MdM), a non-reactive/exhausted MG subcluster in the GBM iTME and an impaired interferon-response signature in the tumor-peripheral cytotoxic cell compartment. Comparing CD8<sup>+</sup> T cells from the tumor periphery to PBMC-derived CD8<sup>+</sup> T cells of the same patient revealed CX3CR1<sup>high</sup> and CX3CR1<sup>int</sup> CD8<sup>+</sup> T cell populations with effector and memory phenotype, respectively. These cells were enriched in the PBMC but lacking in the tumor periphery. Tumor peripheral CD8<sup>+</sup> T cells shared features with tissue-resident memory CD8<sup>+</sup> T-cells with exhausted effector functions.

**Conclusions:** Our analysis provides a large-scale dissection of GBM-associated cell types complemented by patient-matched PBMCs, serving as a high dimensional reference map of the human GBM iTME.

P016

## Swiss Prospective Autologous Bone Flap Resorption Study (SPARS): An Update

A. Stauffer

Signau, Switzerland

**Aim:** Resorption of bone flap after reimplantation following decompressive hemicraniectomy is a well-known problem. Due to mostly short follow-up after reimplantation, the event is likely underreported in the literature. We aim at quantifying the risk of bone flap resorption within the first two years after reimplantation and currently provide a single-site interim-analysis of screening- and study data.

**Methods:** So far, we screened 192 patients that underwent decompressive hemicraniectomy in our institution between Sept 2014 and April 2022 as well as the clinical and radiological follow up one resp. two years after reimplantation of the autologous bone flap. Patients after reimplantation were prospectively enrolled. We performed a 1 resp. 2 year follow up including clinical examination and CT scan. Resorption was classified using a score taking into account clinical (palpable dehiscence, instable flap) and radiological (thickness of flap and dislocation on CT scan) findings. Furthermore, facial symmetry was optically evaluated.

### Results

- Out of 192 hemicraniectomies, 129 (67%) got reimplanted.
- Mortality after decompressive hemicraniectomy: 25.5%.
- 102 patients (53%) agreed to participate in the study. Of those, 65 fulfilled their 12 Mo F/U, whereas 21 (32%) showed bone flap resorption at 12 months after reimplantation. Amongst those who completed the 24 Mo F/U (53 patients), 21 patients (40%) presented with significant bone flap resorption.
- Mean patient age: 52.4 y.
- Mean duration to reimplantation: 2.9 month.

- Indication: CVI (39 patients), SAB (44), aSDH (64), ICB (16), others (29).
- Complications amongst survivors: 6.9% surgical site infections, 2.3% hydrocephalus, 5.6% postoperative hematoma.

**Conclusions:** Decompressive Hemicraniectomy is a treatment of last resort, which explains the high mortality rate. Amongst survivors, cumulated complication rates after reimplantation of the bone flap are 14.8% (surgical site infections, hydrocephalus, postoperative hematoma). 32% of patients show bone flap resorption 1 year after implantation. This results in an overall complication rate of 46.8% within one year after reimplantation. Use of CAD-based patient specific implants instead of autologous bone flaps is a viable alternative after decompressive hemicraniectomy, especially in patients of younger age or in case of segmented bone-flaps due to an even more frequent resorption of the bone flap reported in the literature, requiring additional surgery in the future.

P017

### Innovation of Techniques for Safe Neurosurgery: Quantitative Functional Brain Mapping Imaging Using Arterial Spin Labelling

GR. Iannotti <sup>1</sup>, I. Naudin <sup>2</sup>, V. Ivanova <sup>2</sup>, Q. Tourdot <sup>3</sup>, S. Momjian <sup>2</sup>, K. Lovblad <sup>4</sup>, K. Schaller <sup>2</sup> and F. Grouiller <sup>5</sup>

<sup>1</sup> University Hospital of Geneva, Department of Radiology and Medical Informatics, Department of Neurosurgery, Geneva, Switzerland

<sup>2</sup> University Hospital of Geneva, Department of Neurosurgery, Geneva, Switzerland

<sup>3</sup> University of Montpellier, Faculty of Pharmacy, Montpellier, France

<sup>4</sup> Department of Radiology and Medical Informatics, Geneva, Switzerland

<sup>5</sup> University of Geneva, Laboratory of Behavioral Neurology and Imaging of Cognition, Department of Fundamental Neuroscience, Geneva, Switzerland

**Aims:** Blood Oxygenation Level Dependent (BOLD) is by far the most used contrast for functional MRI [1,2]. However, its spatial specificity can be biased by altered neurovascular coupling, which is typical in patients who are candidate for neurosurgery [3–6]. Arterial Spin Labelling (ASL) is a non-invasive MRI technique for a direct and quantitative measurement of the cerebral blood flow. It can be used for functional imaging as an alternative to the standard BOLD. This work aims to assess the spatial specificity of functional-ASL (fASL) in respect to BOLD and in comparison with Transcranial Magnetic Stimulation (TMS) in healthy subjects, for and before translating fASL in the clinical pre-surgical workflow.

**Methods:** Thirty healthy volunteers ([18–31,40–65] years old, 15 females) performed a motor and somatosensory task in a 3T MRI, while BOLD and ASL were simultaneously acquired. TMS for the representation of ‘hand’ in the brain was performed in a separate session. For each subject and each hand, the coordinates of the global maxima for BOLD and fASL were collected at individual level and then compared with TMS (assumed as ‘gold standard’). To detect systematic shift in the localization, paired-*t*-tests were performed: i) between the two MRI modalities; ii) between TMS and each MRI modality.

**Results:** For the motor task: (i) fASL localized significantly more anteriorly and deeper than BOLD ( $p < 0.05$ ) and (ii) fASL was significant closer than BOLD to TMS ( $p < 0.05$ ), along the posterior-anterior and ventral-dorsal directions. For the somatosensory task, at a group level, fASL localized: (i) more towards the midline; (ii) more anteriorly; (iii) deeper than BOLD.

**Conclusions:** Our results are concordant with the literature which used different types and techniques of analysis [7,8]. The validation step on a selected clinical population will enrich our investigation of fASL spatial accuracy given the availability on perioperative monitoring. In the future, fASL could be a valid and more specific substitution of BOLD, particularly for clinical localization of eloquent cortex to be preserved during brain surgery.

## References

1. Ogawa S et al., 1992. PMID: 1631079.
2. Kwong KK et al., 1992. PMID: 1608978.
3. Jacobs J et al., 2009. PMID: 19349236.
4. Carusone LM et al., 2002. PMID: 12169483.
5. Pittau, F et al., 2013. PMID: 23793553.
6. Agarwal S et al., 2016. PMID: 26201672.
7. Lascano AM et al., 2014. PMID: 24463494.
8. Diekhoff S et al., 2011. PMID: 20533563.

P018

## Quantitative Analysis of the MGMT Methylation Status of Glioblastomas in the Light of the 2021 WHO Classification

L. Häni <sup>1</sup>, M. Kopcic <sup>1</sup>, M. Branca <sup>2</sup>, A. Schütz <sup>1</sup>, M. Murek <sup>1</sup>, N. Söll <sup>1</sup>, E. Vassella <sup>1</sup>, A. Raabe <sup>1</sup>, E. Hewer <sup>3</sup> and P. Schuch <sup>1</sup>

<sup>1</sup> Inselspital, Bern University Hospital, Switzerland

<sup>2</sup> CTU University of Bern, Switzerland

<sup>3</sup> Lausanne University Hospital and University of Lausanne, Switzerland

**Background:** Glioblastomas with methylation of the promotor region of the O(6)-methylguanine-DNA methyltransferase (MGMT) gene exhibit increased sensitivity to alkylating chemotherapy. Quantitative assessment of the MGMT promotor methylation status might provide additional prognostic information. The aim of our study was to determine a quantitative methylation threshold for better survival among patients with isocitrate dehydrogenase (IDH) wildtype glioblastomas.

**Methods:** We included consecutive patients “≥18” years treated at our department between 11/2010 and 08/2018 for a glioblastoma, IDH wildtype undergoing quantitative MGMT promotor methylation analysis. Quantitative MGMT promotor methylation analysis was performed using a primer extension-based method adapted to formalin-fixed paraffin-embedded tissues. Six diagnostically relevant CpG dinucleotides are mapped with this assay. The primary endpoint was overall survival. In a secondary analysis including only tumors exposed to temozolomide (TMZ), the percentage of methylation of each tumor was plotted on a ROC curve using survival “>13.0” months, referring to a historical cohort treated by radiotherapy only, as outcome parameter.

**Results:** 321 patients were included. Mean age was 64.1 years (±11.4). Median overall survival was 12.6 months. Kaplan-Meier and adjusted Cox regression analysis showed better survival for the groups with 16–30% ( $p = 0.010$ ), 31–60% (“ $p < 0.001$ ”), and 61–100% (“ $p < 0.001$ ”) methylation. In contrast, survival in the group with 1–15% methylation was similar to that with unmethylated promotor regions ( $p = 0.204$ ). The secondary analysis confirmed this threshold with a maximal Youden index at “≥ 16%” methylation.

**Conclusions:** Better survival is seen in patients with glioblastomas with “≥16%” methylation of the MGMT promotor region than with “<16%” methylation. Survival with tumors with 1–15% methylation is similar to with unmethylated tumors. Above 16% methylation, we found no additional benefit with increasing methylation. We suggest using the 16% threshold of MGMT methylation for selecting patients in clinical trials and for prognostic counseling.

P019

## A Deep Brain-Computer Interface Enables Parkinson Patients to Reduce Pathological Deep Brain Oscillations and Bradykinesia through Neurofeedback

O. Bichsel <sup>1</sup>, L. Stieglitz <sup>1</sup>, M. Oertel <sup>1</sup>, C. Baumann <sup>1</sup>, L. Imbach <sup>2</sup> and R. Gassert <sup>3</sup>

<sup>1</sup> University Hospital Zurich, Switzerland

<sup>2</sup> Swiss Epilepsy Clinic, Klinik Lengg AG, Switzerland

<sup>3</sup> ETH Zurich, Switzerland

**Aims:** Patients with Parkinson's disease (PD) suffer from symptoms that have been linked to increased beta-oscillatory activity (13–35 Hz) in the basal ganglia. Current state-of-the-art treatments include dopamine replacement therapy and deep brain stimulation (DBS). While these approaches reduce pathological beta-oscillatory activity concomitantly with improving motor performance, we set out to explore deep brain-computer interfaces that exploit neurofeedback to modulate pathological deep brain activity. Neurofeedback has emerged as a promising technique enabling the self-regulation of cortical (EEG neurofeedback) or subcortical brain activity (rt-fMRI neurofeedback). However, while the latter allows subcortical brain modulation, it is inherently slow as it relies on the BOLD response.

**Methods:** We present a much faster method, namely deep brain electrical neurofeedback, which uses implanted DBS electrodes. These measure local field potentials within the subthalamic nucleus that can instantly be processed to provide real-time visual neurofeedback of pathological subthalamic beta activity.

**Results:** All PD patients in this study ( $n = 8$ ) were able to reduce on-going beta-oscillatory activity within as little as 6 min of neurofeedback training ( $p = 0.00092$ ) as compared to their resting beta-activity. We also observed improvement over three consecutive neurofeedback blocks, assessed by a stronger reduction of beta-oscillatory activity by the end of a single training session over one hour as well as accelerated hand movements. Lastly, control over deep brain activity was possible even after removing visual neurofeedback ( $p = 0.0156$ ), suggesting that neurofeedback-acquired strategies to control deep brain oscillations are retained.

**Conclusions:** In summary, we show that deep brain electrode-guided neurofeedback is an efficient way to reduce pathological deep brain activity as well as bradykinesia and that the modulatory effect improves with training and can even be retained once neurofeedback is no longer provided. Further improvement of deep brain neurofeedback might benefit patients with PD by improving symptom control or even patients that suffer from other diseases that DBS is currently tested for.

P020

## Reducing the Learning Curve of Interlaminar Full-Endoscopic Discectomy: Mushroom Model-Simulation Training

A. Simonin <sup>1</sup>, S. Troxler <sup>2</sup> and J. Fournier <sup>1</sup>

<sup>1</sup> Hôpital de Sion, Switzerland

<sup>2</sup> Stöckli Medical AG, Switzerland

**Objective:** To describe a cheap simulation model used to reduce the learning curve of the interlaminar full-endoscopic discectomy.

**Background:** The very difficult learning curve remains one of the main obstacles against the widespread diffusion of interlaminar full endoscopic lumbar discectomy (ILFED). One solution to overcome this learning curve is training with deliberate practice. As realistic models are relatively expensive and cadaver workshops not readily available, we developed a simple and cheap model to train the key steps of the procedure.



**Methods:** A simple and cheap model was designed. It consists of a king oyster mushroom stalk, a glove finger, a sponge and cotton wool. In order to fix the model to the table and to simulate the level of the patient's skin whereupon the hand of the surgeon relies, a wooden holding device was also used.

**Results:** The model has been tested by colleagues attending an advanced ILFED training course on expensive realistic models. A step-by-step learning method with key steps was used. All colleagues evaluated the model as comparable and enough realistic to train key steps in order to reduce the learning curve and training costs.

**Conclusions:** We present an affordable, simple and reproducible training model, which allows for deliberate practice of the key steps of the ILFED procedure. The model may be used by surgeons starting with spinal endoscopy before practicing on more expensive training material, such as realistic models or cadavers.

P021

## Deep Learning Assisted Identification of Shunt Valves on X-ray Images

T. Rhomberg <sup>1</sup>, A. Hakim <sup>2</sup>, A. Raabe <sup>1</sup> and M. Murek <sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Inselspital, Bern University Hospital, Switzerland

<sup>2</sup> Department of Neuroradiology, Inselspital, Bern University Hospital, Switzerland

**Objective:** Over the recent decades, the number of different manufacturers and models of cerebrospinal fluid shunt valves constantly increased. Proper identification of shunt valves on x-ray images is crucial to neurosurgeons and radiologists to derive further details of a specific shunt valve, such as opening pressure settings and MR scanning conditions. The main aim of this pilot study is to evaluate the feasibility of an AI-assisted shunt valve detection system.

**Methods:** The dataset used contains 1444 anonymized images of five different, commonly used shunt valve types from a single institution. All images were acquired from skull x-rays or scout CT-images and were cropped in a random size containing the shunt valve. In detail, the dataset contains images of 359 Miethke proGAV 1, 394 Miethke proGAV 2, 308 Codman Hakim Programmable, 304 Medtronic PS Medical Strata and 80 Integra DP valves. The images were randomly split into a 80% training and 20% validation set. An implementation in Python with the FastAi library (Howard J. et al. 2020) was used to resize all images to 460 × 460 pixels and to train a convolutional neural network with 101 layers using a transfer learning method on a pre-trained model.

**Results:** Overall, our model achieved an F1-score of 0.98 to predict the correct shunt valve model. Breaking down the performance metric for each shunt valve, we could achieve an F1-score of 0.97 for the Codman Hakim Programmable, 0.97 for the Medtronic PS Medical Strata, 0.98 for the Miethke proGAV 1, 0.98 for the Miethke proGAV 2 and 1.0 for the Integra DP shunt valve on our validation set.

**Conclusions:** This technology has the potential to automatically detect different shunt valve models in a fast and precise way and may facilitate the identification of an unknown shunt valve on X-ray or CT scout images. Our results are in line with recent publications (Sujit et al. 2021) demonstrating the feasibility of AI-assisted shunt valve identification. The current model is able to distinguish between five different shunt valve types. A larger dataset including the most common shunt valve models is required to make proper use of this technology in daily routine.

P022

**Identification of Mechanisms Involved in the Recurrence of Glioblastoma by Transcriptomic, Proteomic and Spatial Profiling Analysis****M. Ritz <sup>1</sup>, T. Shekarian <sup>1</sup>, T. Martins <sup>1</sup>, S. Hogan <sup>1</sup>, P. Schmassmann <sup>1</sup> and G. Hutter <sup>2</sup>**<sup>1</sup> University of Basel, Switzerland<sup>2</sup> University of Basel, University Hospital Basel, Switzerland

**Background:** Glioblastoma (GBM) is the most aggressive and common brain tumor. Despite multimodal therapy which consists of complete tumor removal, chemo- and radiation therapy in most patients, the tumor recurs, and the overall survival of only 14 months remains very poor. To identify tumor-induced immune evasion and treatment resistance mechanisms induced during GBM recurrence, we aimed at characterizing the immunological/molecular changes in patient-matched treatment-naïve and recurrent GBM samples.

**Material and methods:** Proteins and total RNA were extracted from 16 patient-matched treatment-naïve (primary) and recurrent GBM fresh frozen tumor samples. The expression of genes involved in brain immune responses were compared using Nanostring panels encompassing Cancer and Neuroinflammation genes. Proteomic was conducted using 6 patient-matched primary and recurrent tumor samples. Immunostaining was performed on a tissue microarray containing matched primary and recurrent tumor samples to identify tumor cells and microglia in order to assess spatial transcriptome of these specific cell types in situ using GeoMX technology. Moreover, correlation analysis of differentially genes and proteins with time to relapse was performed.

**Results:** Genes significantly differentially expressed between primary and recurrent tumors revealed genes overexpressed in recurrent tumors belonging to “FCGR-mediated Phagocytosis” and “synapse pruning” pathways. Proteomic confirmed the synaptic signalling considering overexpressed proteins. Correlation studies with the time to relapse indicated that higher expression of FCG receptors, complement molecules and synaptic components correlate with shorter time to relapse, sharing similarities with neurodegenerative/cognitive disorders such as schizophrenia and Alzheimer disease. The source for these molecules is under evaluation with the spatial transcriptomic analysis.

**Conclusions:** Upregulation of specific proteins such as FCG receptors, complement and synaptic components may result in more favourable conditions for tumor regrowth and may therefore be identified as negative predictors patient outcome. Interfering with these molecules may represent novel therapeutic options after initial GBM surgery.

P023

**Deployment of Stent Retrievers in a Porcine Vasculature Using Robotic Magnetic Navigation****M. Mattmann <sup>1</sup>, P. Gruber <sup>2</sup>, Q. Boehler <sup>1</sup>, S. Gervasoni <sup>1</sup>, C. Chautems <sup>1</sup>, J. Berberat <sup>2</sup>, L. Remonda <sup>2</sup> and B. J. Nelson <sup>1</sup>**<sup>1</sup> ETH Zurich, Switzerland<sup>2</sup> Cantonal Hospital Aarau, Switzerland

**Aims:** Endovascular treatment (EVT) of large vessel occlusion in acute ischemic stroke is the current gold standard. EVT using a magnetic steerable catheter (MSC) is a potential alternative to well-established manual guidewire-based EVTs to directly steer the MSC with a magnetic field. Robotic magnetic navigation systems (MNS) can simplify catheter navigation and allow for remote intervention. This has the potential to reduce procedure

time and costs and also provide treatment in remote areas without specially trained medical staff.

**Method:** A diagnostic MSC was developed and tested in combination with established thrombectomy devices (TD) from Medtronic, Stryker, and Microvention. The catheter has two magnets at the tip and was operated with an MNS and a motorized advancer unit. In-vivo experiments were performed in vivo on a 45 kg pig. The catheter position was tracked with a Philipps Allura Xper FD20 angiography system.

**Results:** The navigation of the MSC and the TD deployment were successfully tested in this in-vivo feasibility study. The MSC has been successfully navigated to different arterial branches of the extracranial vasculature and the TDs have been successfully deployed. Technically, the generated magnetic torque was sufficient to reliably navigate while low enough to avoid arterial damage.

**Conclusions:** This in-vivo study demonstrates the feasibility of MSC navigation in small vessels and the successful deployment of different TDs in an in-vivo model. Future studies need to incorporate remote operation functionality including the remote control of the patient bed and fluoroscope to make this technology suitable for clinical use.

P024

### Super-Selective Angiography and Robotic Navigation in a Porcine Vasculature Using a Magnetic Micro-Catheter

R. Dreyfus <sup>1</sup>, P. Gruber <sup>2</sup>, Q. Boehler <sup>1</sup>, S. Gervasoni <sup>1</sup>, C. Chautems <sup>1</sup>, J. Berberat <sup>2</sup>, L. Remonda <sup>2</sup> and B. J. Nelson <sup>1</sup>

<sup>1</sup> ETH Zurich, Switzerland

<sup>2</sup> Aarau Cantonal Hospital, Switzerland

**Aims:** A newly developed magnetic steerable micro-catheter (MSM) controlled by an electromagnetic navigation system (eMNS) offers remote control and high navigability in small and distal vessels. Currently, endovascular therapy (EVT) of distal vessel occlusion (DVO) in acute ischemic stroke (AIS) is increasingly performed (1). Endovascular treatment of DVO requires a high degree of technical expertise and is not without risk. Here, we present a novel concept of MSM that can be applied to AIS patients with DVO using intra-arterial thrombolysis (IAT).

**Method:** A 2Fr micro-catheter with magnetic tip was navigated through the small branches of the external carotid artery (ECA) of a 45 kg pig in vivo. The MSM tip was controlled with means of external magnetic fields generated by an (eMNS) and advanced by a motorized advancer. The operator interacted with the system via a hand-held controller. The MSM was imaged using a mono-planar angiography system (Philipps Allura Xper FD20). Once the target site was reached, a IAT mimicking contrast agent solution (50:50 Iopamiro 300) was injected.

**Results:** The MSM was successfully navigated in small diameter, tortuous vessels (small branches of the ECA). An injection of contrast agent was performed at multiple target sites imitating IAT application. The magnetic catheter showed high controllability for selecting multiple millimetre-sized arteries.

**Conclusions:** We demonstrated the feasibility of MSM using eMNS in small vessels in a porcine model. Due to the ease of use of this novel technique, MSM has the potential to facilitate EVT in AIS patients by reaching more distant vessel occlusions and addressing complex anatomical situations.

P025

**Personalized Predictive Modeling of Epileptic Network Dynamics****T. Dubcek**<sup>1</sup>, **D. Ledergerber**<sup>2</sup>, **F. Capecchi**<sup>3</sup>, **M. Serra Garcia**<sup>4</sup>, **R. Polania**<sup>5</sup> and **L. Imbach**<sup>2</sup><sup>1</sup> ETH Zurich/Swiss Epilepsy Clinic, Switzerland<sup>2</sup> Swiss Epilepsy Clinic, Switzerland<sup>3</sup> University Hospital Zurich, Switzerland<sup>4</sup> AMOLF, Netherlands<sup>5</sup> ETH Zurich, Switzerland

**Aims:** Epilepsy research has recently undergone a paradigm shift: from epilepsy as focal cortical disease towards epilepsy as network disease. This is motivated by new evidence of widespread brain activity in seizure initiation and maintenance, and by promising results of brain stimulation for drug-resistant cases. However, a thorough understanding of the network-rooted epileptic dynamics is still missing, and the details of the stimulation procedures do not account for the variable brain network dynamics between patients.

**Methods:** We develop personalized dynamical models of epileptic networks, based on EEG in an entirely data-driven manner. A dynamic connectivity matrix, simultaneously capturing the dominant spatial and temporal modes in the epileptic network, is extracted for steady-state EEG dynamics. The considered population includes 30 patients with frequent epileptiform discharges ("active EEG"). The dynamical properties of the active and inactive EEG states are compared.

**Results:** Our model accurately reproduces the clinically relevant properties of the recorded EEG dynamics: spectral power, channel coherence and amplitude variation. We find the dominant coherent structures for each epileptic network state. In addition, the models allow to simulate the effects of external network stimulation. By comparing the two types of brain dynamics, the model is used to predict targeted interventions to transition from pathological to healthy states.

**Conclusions:** We developed personalized EEG-driven models of epileptic network dynamics. We demonstrated their accuracy for patients with active EEG. The models can be readily used to predict the optimal localization and stimulation parameters of patient-specific interventions and help resolve the pathological epileptic network states.

P026

**Neural Interaction Dynamics between the Anterior Thalamus and the Cortex in Epilepsy Patients****G. Aiello**<sup>1</sup>, **L. Stieglitz**<sup>2</sup>, **C. Baumann**<sup>3</sup>, **R. Polania**<sup>1</sup> and **L. Imbach**<sup>4</sup><sup>1</sup> ETH Zurich, Switzerland<sup>2</sup> Department of Neurosurgery, USZ, Switzerland<sup>3</sup> Department of Neurology, USZ, Switzerland<sup>4</sup> Swiss Epilepsy Center, Klinik Lengg, Switzerland

Due to its connectivity profile and its potential role in the subcortical propagation of seizures, the Anterior Nucleus of the Thalamus (ANT) is chosen as the stimulation target in Deep Brain Stimulation (DBS) for drug-resistant epilepsy (DRE). We aimed to analyze how the ANT interacts with the neocortex and to explore the electrophysiological mechanisms underlying the effectiveness of this method.

Electroencephalograms (EEG) and ANT Local Field Potential (LFP) have been recorded parallelly during the intra-operative phase of ANT-DBS bilateral implantation in 15 subjects. High-frequency test stimulations in the ANT have been delivered, while EEG was recorded.

Firstly, by analyzing the electrophysiological properties of the ANT in the spectral domain, we found that the major difference among thalami ( $T = 30$ ) was observed in the theta and low alpha range. The same result was found along the implantation trajectory. A sweet-spot of a higher theta power was found at approximately 1.5 to 3.5 mm post-entry. The strongest connectivity (wpli-debiased) between the scalp and ANT bilaterally was found in the theta band (N-way ANOVA,  $p < 0.01$ ), with F3/F4 channels most strongly connected to left/right ANT respectively. Importantly, the depth of recording of the ANT along the implantation trajectory did not affect the profile of connectivity to the cortical regions. We analyzed EEG properties with ("ON") and without ("OFF") stimulation (paired  $t$ -test). A significant decrease ( $p < 0.05$ ) in high beta and gamma power was found and spread throughout the scalp, counteracted by a trend towards an increase in lower frequencies. Scalp Connectivity showed a statistically significant increase (ON-condition) in the theta band and in the gamma band ( $p < 0.001$ ).

We finally explored how these measures correlated to subjective responsiveness to therapy, computed as the reduction in seizure frequency 6 months post-implantation. We divided our cohort of patients into Responders ( $N = 9$ ) and Non Responders ( $N = 6$ ). We found that Responders presented a significantly stronger scalp and ANT theta power, both in OFF and ON conditions. Moreover, the average ANT to scalp theta connectivity was stronger in Responders than in Non Responders, with a focus on fronto-central areas. In conclusion, this study represents an unprecedented characterization of the dynamical interactions between the ANT and the cortex in the context of ANT DBS for DRE, providing crucial information to optimize this therapy.

P027

### Probing Cortical Excitability under GABAergic Modulation in Humans with Epilepsy

E. van Maren <sup>1</sup>, J. Anso <sup>2</sup>, M. Fuchs <sup>1</sup>, W. Z'Graggen <sup>1</sup>, K. Schindler <sup>1</sup>, C. Pollo <sup>1</sup> and M. Baud <sup>1</sup>

<sup>1</sup> Inselspital–Universitätsspital Bern–Universitätsklinik für Neurologie, Switzerland

<sup>2</sup> ARTORG Center for Biomedical Engineering, University of Bern, Switzerland

**Background:** In focal epilepsy, seizures result from subnetworks of abnormally high cortical excitability (CE) within a relatively normal brain. Practical means of monitoring CE in the human brain, for example to assess the effects of anti-seizure medications are currently lacking. We asked whether directly probing the brain with minute electrical pulses and recording cortico-cortical evoked potentials (CCEPs) may help quantify CE before and after administration of a benzodiazepine (BZD).

**Methods:** In seven epilepsy patients undergoing cortical recordings for diagnostic reasons (median number of electrode contacts: 68 [48, 111]), we probed CE with repeated single pulses (median  $N = 168$  [151, 204]) systematically varying in intensity (0.2–12 mA). All brain responses, before and after administration of clonazepam (0.75–1 mg) were clustered into subnetworks using NMF (Non-negativity matrix factorization) based on the dynamics of CCEPs. CE in each subnetwork was quantified by the magnitude of the NMF activation coefficients.

**Results:** Across patients, NMF delineated a total of 20 subnetworks that encompassed a collection of brain areas with shorter- and longer-range connections responding conjointly to the administered probing stimulations with CCEPs. Across these subnetworks, CE was significantly decreased after BZD administration (Wilcoxon signed-rank test:  $p = 0.0003$ ).

**Conclusions:** Combining probing neurostimulations with unsupervised pattern recognition algorithms, we introduce a novel method to quantify CE in the human brain. As a proof-of-principle, we apply this method to uncover the network effects of a well-known GABA agonist on CE. Applying such methods over longer durations, may help monitor non-linear dynamics in the human cortex, including in epilepsy.

P028

### Antiseizure Medication within 48 h after the First Seizure Provides Better Seizure Control than Later Treatment

E. Ménétré, P. De Stefano, M. Seeck, P. Mégevand, F. Sarasin, M. Vargas and A. Kleinschmidt

University Hospitals of Geneva, Switzerland

**Objectives:** In this retrospective single-center study, we examined the impact of delay of anti-seizure medication (ASM) introduction on outcomes for patients with new-onset epilepsy (NOE), starting in the emergency department (ED).

**Methods:** All patients ( $\geq 16$  years) with NOE between 1.3.2010 and 1.3.2017 were included in the present study. The diagnostic protocol included routine EEG, brain CT/MRI, long-term overnight EEG (LT-EEG) and specialized consultations, which were launched as soon as the patient arrived in the ED. Patients were followed for 5 years. The effect of the delay of treatment introduction on the relapse rate was investigated using Cox proportional hazard models. Potential confounded variables such as the presence of a tumor, the type of epilepsy, the sex, etc. were controlled for in the models.

**Results:** 487 patients suffered from NOE. If treatment was initiated  $\leq 48$  h, relapses were less likely as compared to patients with ASM introduction  $> 48$  h (39.4% vs. 68.1%, respectively,  $p < 0.001$ ). Patients with a history of anterior events ( $p < 0.001$ ), male sex ( $p = 0.003$ ), younger patients ( $p = 0.04$ ) and focal epilepsy ( $p = 0.04$ ) were more likely to relapse. Despite these variables controlled for, the effect of treatment delay remained highly significant, and if only patients with full treatment by 6 months were considered, the effect remained significant as well ( $p < 0.001$ ).

**Conclusions:** Our results suggest the benefit of swift work-up and introduction of ASM therapy within 48 h after the first seizure. ASM therapy within 48 h was associated with better prognosis up to 5 years after the index event. Patients may benefit of first-seizure units, similar to stroke units, activated upon arrival in the ED as well the development of more ASM allowing rapid up-titration.

P029

### Acute Symptomatic Seizures in Stroke: The Onset of Epilepsy?

Patrick Stancu, Pia De Stefano, Maria Vargas \*, Eric Menetre, Emmanuel Carrera, Andreas Kleinschmidt and Margitta Seeck

Neurology Division and \* Neuroradiology Division, University Hospital of Geneva, Switzerland

**Objective:** Hippocampal sclerosis (HS) is a prominent biomarker of epilepsy. If acquired later in life, it usually occurs in the context of degenerative or acute inflammatory-infectious disease. Conversely, acute symptomatic seizures (ASS) are considered a risk factor for developing post-stroke epilepsy but other factors remain unrecognized. Here, we hypothesize that silent hippocampal injury contributes to the development of post-stroke epilepsy.

**Methods:** We performed a retrospective observational study of patients hospitalized between 1/2007 and 12/2018 with an acute stroke in the Stroke Center of the Geneva University Hospital. Patients were included if they had a documented normal hippocampal complex at onset and a control MRI at  $\geq 2$  years interval without new lesion in the meantime.

**Results:** 162 patients fulfilled our inclusion criteria. ASS during the first week ( $p < 0.0001$ ) and epileptiform abnormalities in electroencephalography (EEG;  $p = 0.02$ ) were more frequently associated with the development of epilepsy. Hemorrhagic stroke was strongly

associated to both ASS and future focal epilepsy ( $p = 0.00097$ ). Three patients (1.8%) developed hippocampal sclerosis ipsilateral to the cerebrovascular event between 2 and 5 years, all with ASS and hemorrhagic stroke.

**Interpretation:** ASS and epileptiform EEG abnormalities are strong predictors of post-stroke epilepsy. HS develops in a minority of patients after hemorrhagic lesions, leading to focal epilepsy. Prospective studies are required, including systematic follow-up with EEG and if characterized by epileptiform discharges, with MRI, to determine the true frequency of HS and predictors of post-stroke epilepsy (AAS, stroke type, HS), and eventually, its impact on stroke recovery.

P030

### Temporal Lobe Epileptogenesis Implies Large-Scale Dynamics in a Status Epilepticus-Induced Mouse Model

F. Friscourt <sup>1</sup>, V. Ferat <sup>1</sup>, M. Hernot <sup>1</sup>, K. Schaller <sup>2</sup>, C. Michel <sup>1</sup> and C. Quairiaux <sup>1</sup>

<sup>1</sup> University of Geneva (UNIGE), Switzerland

<sup>2</sup> HUG Hôpitaux Universitaires Genève, Switzerland

Temporal lobe epilepsy (TLE) is the most common type of focal epilepsies. While TLE is characterized by the presence of an epileptic focus (EF) that is held to be responsible for triggering seizures and driving interictal activities, recent studies showed that epileptogenic networks (EN) and brain alterations are widely distributed, even in well diagnosed focal epilepsies. The pathologic mechanisms that drive the development of the EN are unclear, led us to investigate two possibilities: does the EF pathological activities disrupted distant brain regions and trigger the EN formation or, does the EN development started as soon as the initial insult, and so, before the first apparition of focal epileptic activities.

Using multisite chronic mSEEG recordings and chemogenetic tools in the unilateral intra-hippocampal kainate (KA) mouse of TLE (IHK), we propose to characterize in detail the emergence of epileptic activities in the EF and in remote regions and evaluate the role of the primary epileptogenic region for the development of the large-scale EN. Interestingly, we found that the different types of epileptiform activities, i.e., the various types of ictal, ictal-like or interictal patterns, starts to appear in the very early stage of the epileptogenesis (i.e., at least 72 h after KA injection) in both the EF and the contralateral hippocampus and evolve to become typical epileptic events (seizures, fast-ripples, generalized spikes, etc.). We investigate precisely these network dynamics with high spatial and temporal precision using systematic unbiased detection of pathological activities. Such a detailed description of the pathological activities during this period is fundamental to understand how neuronal networks alterations emerge in lesioned (sclerotic injected hippocampus) and apparently non-lesioned regions. Beyond these important descriptive aspects, we hope to further identify key mechanisms of epileptic neuronal networks development.

P031

### Alteration of Gamma Oscillations Correlates with Cortical Tau Deposition in Alzheimer's Disease

U. Nench <sup>1</sup>, I. Rigoni <sup>2</sup>, F. Ribaldi <sup>2</sup>, S. Tomczyk <sup>2</sup>, I. M. Constantin <sup>2</sup>, S. Vulliémaz <sup>3</sup>, M. Seeck <sup>3</sup>, V. Garibotto <sup>3</sup>, G. Frisoni <sup>3</sup> and D. Altomare <sup>2</sup>

<sup>1</sup> Hôpitaux Universitaires de Genève, Switzerland

<sup>2</sup> University of Geneva (UNIGE), Switzerland

<sup>3</sup> Geneva University Hospitals (HUG) and University of Geneva (Unige), Switzerland

In Alzheimer's disease, cortical tau deposition has been associated to synaptic density loss, neurodegeneration, and cognitive decline. A deficit in gamma oscillations has been observed on EEG of AD patients. Loss of gamma oscillations is considered a marker of GABAergic interneuron dysfunction and synaptic loss. We explored the correlation between alterations of gamma oscillations and cortical tau deposition in AD patients. We selected 18 patients from the Geneva Memory Center dataset who underwent tau-PET, amyloid-PET and a 25-electrode scalp resting-state EEG. We estimated the power spectral density on 30 epochs of one second and power in the gamma frequency band (30–100 Hz). We compared the average gamma power between subjects with and without significant cortical tau deposition. We correlated the localization of tau standardized uptake value ratio (SUVR) with power distribution of gamma oscillations in both groups. Of the 18 included patients, 9 had positive tau-PET and amyloid-PET scans. Of these, 5 (56%) showed a more prominent tau burden in the left temporal and parietal lobes, with the remaining 4 (44%) having a bilateral distribution. Of the 9 negative tau-PET patients, only one had a positive amyloid-PET. We observed a statistically significant decrease of total gamma power in tau-positive compared to tau-negative patients ( $p = 0.038$ ). In tau-positive patients, regional analyses showed a non-significant inverse relationship between tau burden and gamma power (i.e., with increasing tau burden, gamma power decreased). This tendency was strongest in the precuneus, parietal and temporal lobes of the most affected hemisphere on molecular imaging. A non-significant positive correlation was observed in the same lobes of the contralateral hemisphere in tau-positive patients and in both hemispheres of tau-negative patients (i.e., with increasing tau burden, gamma power increased).

Alterations in gamma oscillations could be a biomarker for cortical tau deposition in AD. The opposite relationship between tau burden and gamma oscillations observed in the different hemispheres might represent a large-scale compensatory mechanism in the least affected one. Indeed, recent studies found an increase in beta and gamma oscillations in frontal regions of subjects showing signs of degeneration on FDG-PET. In conclusion, alterations of gamma oscillations might be a promising electrophysiological marker for early diagnosis and possibly follow-up of Alzheimer's disease.

P032

### **The Value of Motor Evoked Potentials in Detecting Mechanical Versus Vascular Injury During Resection of Supratentorial Mass Lesions**

**P. Alvarez Abut, E. Asimakidou, A. Raabe and K. Seidel**

Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland

During surgical resection of supratentorial mass lesions, motor deficits might be caused by different patterns of injury: mechanical (damage of primary motor cortex/corticospinal tract), ischemic (coagulation of perforator arteries, vasospasm), or lesion of associative motor areas. Recently, we performed a scoping review to assess intraoperative motor evoked potentials (MEP) warning criteria (1). Here we present the data of a subgroup of patients, with focus on the pattern of injury.

A systematic search of the literature using PubMed, Embase, Scopus, CINAHL and the Cochrane Library was undertaken. Inclusion criteria were intraoperative electrically elicited MEP with predefined alarm criterion in anesthetized patients undergoing supratentorial brain surgery with quantitative report of motor outcome. For this subgroup analyses we focused on supratentorial parenchymal lesions.

Of the 68 included papers, 54.8% described the different intraoperative injury patterns. For permanent deficits, 2 groups described exclusive mechanical injury, 6 exclusive vascular and 8 mixed patterns. For transient deficits, 3 groups described exclusive mechanical injury, 1 exclusive vascular and 3 mixed patterns. Of 1551 cases, there were



7.8% of permanent motor deficits (3.2% mechanical, 2.6% vascular, and 1.9% of unclear cause). For mechanical injury 38, 6 and 4 cases had irreversible, reversible and no change of MEP, respectively; whereas for vascular injury the corresponding numbers were 30, 5, and 5. For transient motor deficits, 27 cases were due to mechanical injury, of which 9 had irreversible, 1 reversible and 17 no change of MEP. For vascular injuries (12 cases) the corresponding numbers were 4, 5 and 3, respectively, with more reversible changes in vascular than mechanical cases ( $p = 0.01$ —Chi square test).

In the group of patients with transient postoperative motor deficits, the subgroup with vascular injury had significantly more reversible MEP changes than the mechanical injury patients. This suggests that an MEP alert may reduce permanent motor deficits caused by vasospasm/transient ischemia. In the whole group, we observed a slight predominance of mechanical injury. Thus, additional subcortical mapping strategies may improve surgical guidance. Deeper understanding of the mechanisms of injury could help to develop a strategy for a faster and more effective detection of an intraoperative lesion, as well as the suggested methodology to avoid permanent deficits.

P033

### Peripheral Neuropathy Following COVID-19 mRNA Vaccination—2 Case Reports

P. Dorin, D. Leupold, A. Felbecker and T. Hundsberger

Kantonsspital St. Gallen, Switzerland

**Introduction:** We describe two recent cases of peripheral neuropathy reported after vaccination with mRNA SARS-CoV2 vaccine (Moderna®).

**Methods:** The first patient developed a neuralgic amyotrophy, the second patient a radial neuropathy.

**Results:** A 67-year-old man with hypertension and hyperlipidemia developed acute and severe neuropathic shoulder pain 8 days after the second vaccination dose of COVID-19 vaccine in the ipsilateral deltoid muscle. A causative trauma and other differential diagnoses were denied. NSAIDs showed no effect, but corticosteroids improved the pain. Subsequently paresis of the left proximal shoulder muscles occurred, and EMG showed axonal damage. A 60-year-old female with no medical history developed weakness of left hand extension 4 days after the first vaccination dose of COVID-19 vaccine in the ipsilateral deltoid muscle. Neurological examination showed a mild paresis of the radial innervated muscles in the forearm and reduced sensitivity of the dorso-radial area of her hand. Nerve-conduction-studies demonstrated a conduction block of the radial nerve proximal to the elbow, concomitant with focal swelling detected by high-resolution nerve ultrasound.

**Conclusions:** The two cases show a temporal and local association (ipsilateral injection) of peripheral neuropathies after vaccination with mRNA COVID-19 vaccine (Moderna®). Similar case reports are published. However, temporal association is not equal to causal association and can ideally be investigated by prospective randomized trials, which is unethical in the pandemic situation. Therefore, prospective register studies, case series and case reports must act as a substitute. However, due to underreporting or insufficient timely data processing a large body of information is missing.

P034

### Diagnostic Value of Blink Reflex Latencies for Patients with Idiopathic Trigeminal Neuralgia

T. Badel <sup>1</sup>, V. Basic Kes <sup>2</sup>, D. Zadavec <sup>2</sup>, S. Kocijan Lovko <sup>3</sup>, I. Savic Pavicin <sup>4</sup> and S. Anić Milošević <sup>1</sup>

<sup>1</sup> School of Dental Medicine, Switzerland

<sup>2</sup> Clinical Hospital Centre “Sisters of Charity”, Croatia

<sup>3</sup> Clinic for Psychiatry St Ivan, Switzerland

<sup>4</sup> School of Dental Medicine, Switzerland

**Objectives:** The aim of this research was to determine the differences in blink reflex latencies as a diagnostic tool for unilaterally idiopathic TN compared with pain-free health volunteers.

**Methods:** A prospective cohort study was conducted over 2 years. The final subgroup TN-Subgroup included 15 patients (mean age/SD 62.3 ± 10.7 years; 10 (66,7%) female). Blink-eliciting stimuli were performed by surface electrodes to stimulate the supraorbital nerve at the forehead. Pain-free and healthy volunteers as a HV-Subgroup (mean age/SD: 30.8 ± 8.1 years; 12 (75%) female) were recruited from asymptomatic students of dental medicine.

Diagnostic parameters were determined by measuring latency (in ms) to the onset of the reflex components from electric stimulation. The shortest latency values obtained were taken into account. They were composed of homolateral early response R1 and bilateral late response R2 (homolateral response), and R2c (contralaterally expressed response), the occurrence of ipsilateral/contralateral R3/R3c component, and side-to-side difference for R1, R2 and R2c latencies. The level of anxiety was evaluated by Spielberger’s psychological measuring instrument State-Trait Anxiety Inventory.

**Results:** A strictly unilateral TN was diagnosed on the right side in 53% patients. There was no difference in sex distribution between NT and HV subgroups (Fischer’s exact test  $p = 0.4815$ ). The following anxiety scores with statistically significance were found comparing TN-subgroup/HV subgroup–STAI 1: 45.06 ± 8.90/31.94 ± 10.25 and STAI 2: 43.12 ± 9.30/35.00 ± 10.11 respectively ( $p = 0.0001/p = 0.009$ ). Blink reflex latencies of stimulation values left and right side together between subgroups were significantly higher for latencies values R1, R2, R2c at TN-subgroup ( $p < 0.05$ ). Other blink reflex parameters were analysed, such as the absence of R1 latency, and the presence of R1c, R3, and R3c latencies.

**Conclusions:** Nociceptive blink reflex is a non-invasive and painless method with the purpose of objectifying neuropathic pain in different groups of patients. Blink-reflex parameters (R1, R2 and R2c) were significantly abnormal not only upon comparing TN-patients with healthy volunteers. The R3 component of the reflex was related to noxious stimuli, likewise by innocuous stimuli.

P035

### Differential Regulation of PBMCs by Plasma-Derived Extracellular Vesicles from Parkinson’s Disease Patients

E. Vacchi <sup>1</sup>, S. Pannella <sup>2</sup>, C. Balbi <sup>2</sup>, L. Barile <sup>2</sup>, A. Kaelin-Lang <sup>2</sup> and G. Melli <sup>2</sup>

<sup>1</sup> EOC, Switzerland

<sup>2</sup> EOC, Switzerland

**Background:** There is extensive and growing evidence about the role of inflammation in Parkinson’s disease (PD). In addition to neuroinflammatory processes occurring in the brain, elevated levels of pro-inflammatory factors are also present in the plasma of PD.

Extracellular vesicles (EVs), secreted membrane particles involved in cell-to-cell communication, carry important information on immunity and its dysregulations. Thus, we hypothesize that plasmatic inflammatory EVs may have a functional role in disease initiation and progression.

**Methods:** Peripheral blood mononuclear cells (PBMC) from healthy donors were incubated for 22 h with PD vs. healthy control (HC) circulating EVs previously labeled with the lipophilic dye DiR. A panel of 14 specific antigens was used to identify more than 12 subpopulations of PBMC by FACS analysis. For each subpopulation, we dissected the differential EV internalization and immune activation. PBMCs were also treated with LPS to mimic an inflammatory condition; the differential EV internalization and immune activation of PBMCs receiving EVs from PD and HC in inflammatory conditions was evaluated. Finally, with a cytokine array on PBMCs media treated with EVs from PD or HC, we evaluated the differential secretion.

**Results:** The exposition with EVs from PD induced an increase in NKT CD80+ cells. In inflammatory conditions, we observed an increased of CD16+ cells in PBMCs treated with EVs from PD. Finally, the exposure to EVs from PD or HC induced a differential release of cytokine by PBMCs.

**Conclusions:** The differential response of PBMCs to EVs derived from PD or HC peripheral blood suggest a differential message carried by EVs. A deep plasma-derived EVs functional analysis may shed light on the role of inflammatory dysregulation in causing PD.

P036

## A Masked Object Recognition Task as an Objective Marker for the Visual Snow Syndrome

C. Schankin <sup>1</sup>, O. Banz <sup>2</sup>, O. Ulrich <sup>3</sup>, A. Klein <sup>4</sup> and M. Ertl <sup>3</sup>

<sup>1</sup> Inselspital — Universitätsspital Bern, Switzerland

<sup>2</sup> Universität Bern, Switzerland

<sup>3</sup> Department of Psychology, University of Bern, Switzerland

<sup>4</sup> Insel Gruppe AG, Inselspital, Universitätsspital Bern, Switzerland

**Introduction:** Visual Snow Syndrome (VSS) is a migraine-related perceptual disorder. The main symptom is “visual snow (VS)” resembling the view of TV-static in the entire visual field. (1) There are additional visual symptoms such as enhanced entoptic phenomena, palinopsia, photophobia and nyctalopia. The diagnosis as established in the ICDH3(2)-criteria is based solely on patient history. Here we propose an objective marker supporting the diagnosis and quantifying VS symptom intensity.

**Methods:** Fourteen subjects (9 VSS, 5 matched healthy controls) participated in a web-based, object recognition task, in which images of common objects were masked with black and white noise, which approximates the quality of VS as reported by the patients. At the beginning of each of the ten trials, the added noise covered the entire image, making object recognition impossible. Over time the noise level was automatically reduced until subjects signaled that they recognized the image embedded in the noise via a button press. To control for correct identification subjects had to select the answer from five alternatives presented on the screen. The primary endpoint was the mean noise level at the moment of recognition. This was compared between the two groups using an independent *t*-test.

**Results:** Comparing the mean detection performance between VSS patients and matched healthy controls, we found a significant difference over all stimuli ( $p = 0.026$ ,  $d = 1.05$ ). Overall detection performance was lower in VSS (mean noise level = 34.27) than in healthy controls (mean noise level = 37.48), demonstrating that people suffering from VSS require a lower level of noise to successfully recognize objects than people without VSS.

**Conclusions:** The preliminary data show that subjects with VSS can be identified by their reduced performance in a masked object recognition task. The presented test provides the first attempt to quantify the severity of VS by an objective measure. In the future, such a test might be used as a diagnostic tool or, to monitor the success of therapeutic interventions, or in research projects

P037

### Response to Fremanezumab in Migraine Patients with and without Prior aCGRP mAbs—Preliminary Data from the FINESSE Study

C. Schankin <sup>1</sup>, G. Broessner <sup>2</sup>, C. Gaul <sup>3</sup>, T. Kraya <sup>4</sup>, X. Hamann <sup>5</sup>, B. Haertel <sup>6</sup>, L. Neeb <sup>7</sup> and A. Straube <sup>8</sup>

<sup>1</sup> Inselspital, Bern University Hospital, Switzerland

<sup>2</sup> Medical University of Innsbruck, Austria

<sup>3</sup> Kopfschmerzzentrum Frankfurt, Germany

<sup>4</sup> St. Georg Hospital Leipzig, Germany

<sup>5</sup> Teva GmbH Ulm, Germany

<sup>6</sup> Teva Pharma AG Basel, Switzerland

<sup>7</sup> Charité Universitätsmedizin Berlin, Germany

<sup>8</sup> Ludwig-Maximilians-University Munich, Germany

**Aims:** According to some guidelines for health insurance reimbursement, ineffective use of one aCGRP mAb (monoclonal antibody targeting the CGRP pathway), defined by not reaching a reduction of monthly migraine days (MMD) by 50% compared to baseline after 6 months of treatment, excludes reimbursement of another aCGRP mAb. The aim of this preliminary analysis is to quantify the effectiveness of switching between aCGRP mAbs due to lack of efficacy of previous aCGRP mAb treatment.

**Methods:** FINESSE is a multicenter, two-country (Germany, Austria) prospective non-interventional study (NIS) in which effectiveness and tolerability of fremanezumab in adults with EM and CM are evaluated in routine clinical practice. Medical history of patients is documented at baseline, including past preventive treatment (PPT) with another aCGRP mAb (erenumab or galcanezumab). This preliminary subgroup analysis (cut-off date 14.05.21) focused on preventive migraine treatments with other aCGRP mAbs prior to initiation of fremanezumab. Distribution of patients with and without ineffective PPT with another aCGRP mAb was analysed for the primary endpoint of FINESSE, the proportion of patients reaching  $\geq 50\%$  reduction in MMD that was evaluated during the 6-month period after the first dose of fremanezumab.

**Results:** 574 patients with fully documented baseline visit were included (89.4% female,  $45.7 \pm 12.2$  years of age); 58.4% had EM, 41.6% CM. Of those, 308 had completed the 6-month visit, 241 without and 67 with prior exposure to another aCGRP mAb. The main reason for discontinuation of prior aCGRP mAb therapy was, according to the patients at baseline visit, lack of efficacy in 57 patients (85.1%) and other reasons in 10 patients (14.9%). In total 150 of 308 patients (48.7%) achieved the primary endpoint of  $\geq 50\%$  reduction from baseline in MMD at month 6 after the first dose of fremanezumab. In the subgroup of patients with lack of efficacy of prior aCGRP mAbs, 18 of 57 (31.6%) reached the primary endpoint and 129 of 241 in patients without prior aCGRP mAb treatment (53.5%).

**Conclusions:** This preliminary data provides prospective real-world evidence that treatment with fremanezumab is effective in about 30% of patients with prior ineffective aCGRP mAb treatment. For these patients, a switch should not be withheld since it can be a promising treatment option.

P038

**ComPAIN—Communication of Pain in Patients with Headache****E. Eicher**<sup>1</sup>, **S. Rätz**<sup>1</sup>, **M. Stattmann**<sup>1</sup>, **E. Neumann**<sup>1</sup>, **H. Pohl**<sup>1</sup>, **Y. Ilg**<sup>2</sup>, **A. Maatz**<sup>3</sup> and **S. Wegener**<sup>1</sup><sup>1</sup> Department of Neurology, University Hospital Zurich and University of Zurich, Switzerland<sup>2</sup> Department of German Studies, University of Zurich, Switzerland<sup>3</sup> Centre for Social Psychiatry, Psychiatric Hospital, University of Zurich, Switzerland

**Aim:** Primary headaches are a common debilitating health condition, affecting more than 1 billion people worldwide. Proper diagnosis and treatment depend on communication. We want to reveal differences in pain communication depending on headache disorder as well as individual patient factors, including sex. Furthermore, we would like to analyze patients' satisfaction with our consultations and evaluate if there is a correlation with communication.

**Methods:** Patients with suspected primary headaches visiting our headache unit were asked to participate. Up to now, we included 18 patients: 10 of them diagnosed with migraine, 3 with tension type headaches (TTH), 3 with both (migraine and tension type headaches (M+TTH)) and 1 with cluster headache. The patients were asked to fill in a questionnaire before entering their consultation, after finishing the consultation and a third questionnaire 6 months later (sent home via mail). We recorded the consultations on video and audio tapes for linguistic analyses.

**Results:** On average, migraine patients used more words to characterize their pain: 22.67 vs. 9 in TTH patients ( $p = 0.286$ ). Migraine patients also tended to use the first-person narrative more often (50% vs. 30% in TTH patients,  $p = 0.648$ ), and showed a slightly better satisfaction with the consultation overall (90.68% vs. 80.93% in TTH patients,  $p = 0.168$ ). However, due to the small patient groups at the current stage these trends were not significant.

**Conclusions:** Our preliminary results suggest that communication of headache differs depending on headache diagnosis and individual patient characteristics. More in depth analysis of a larger patient cohort will be presented at the conference. We hope to make an important contribution to the understanding of our future patients with headache, ultimately leading to better treatments and patient satisfaction.

P039

**A Report of Patient with CNS Vasculitis Relieving of Neurogenic Bowel through Biofeedback****S. Y. Jun**

Seoul St. Mary's hospital, College of Medicine, The Catholic University of Korea, Korea

**Background:** Central Nervous System(CNS) vasculitis is a rare disease that cause inflammation in the vessels of the CNS without evidence of vasculitis outside the CNS. It presents clinical features motor weakness, cognitive problems, and difficulties controlling bladder and bowel incontinence and symptom of neurogenic bowel makes quality of life lower in patients with this diseases. Here, we introduce a case that improved through biofeedback treatment in addition to oral medications for constipation in the young patient with neurogenic bowel who was diagnosed with CNS vasculitis.

**Case Report:** A 28-year-old male represented symptoms of dizziness, gait disturbance, visual disturbance, and dysphagia and was diagnosed with CNS vasculitis with brain MRI. He came to the rehabilitation unit due to worsened dysphagia and gait disturbance. His Modified Barthel Index score was 29 and Mini Mental Status Examination score was 28. Also he complained severe constipation and difficulty with evacuation. There were a

lot of feces in large intestine and rectum on his abdominal x-ray. Although several drug such as oral osmotic or stimulant laxatives and bisacodyl suppository were used, symptoms did not improve. Manometry was performed to differentiate colon transit disorder, and there were no specific findings in colon transit time. We regard his symptom as an anorectal function disorder and recommend the biofeedback treatment. During the 1st time of biofeedback treatment, the patient showed problems with increasing the abdominal pressure or relaxation of external anal sphincter muscle but after 4 times of treatments, he showed improvement in controlling the abdominal pressure and anal sphincter. After that he said it was much easier to defecate and was able to reduce the number of oral medications he took for neurogenic bowel. Afterwards, the patient continues physical, occupational therapy and biofeedback therapy.

**Conclusions:** Bowel biofeedback is a conservative method for neurogenic bowel that brings behavioral changes in the patients with functional chronic constipation or dyssynergic pattern of defecation. Otherwise, there were few reports with biofeedback in stroke or CNS vasculitis patients. If the patient's cognitive function and cooperation are adequate, biofeedback could be an effective treatment option for neurogenic bowel in patients with stroke or central vasculitis.

P040

#### S100 Fails to Predict Post Stroke Epilepsy, Data from BIOSIGNAL Study

G. Biccato <sup>1</sup>, N. Scherrer <sup>1</sup>, M. Arnold <sup>1</sup>, M. Galovic <sup>1</sup>, C. Inauen <sup>1</sup>, A. Luft <sup>1</sup>, T. Pokorny <sup>1</sup>, L. Saleh <sup>2</sup>, V. Schütz <sup>1</sup>, J. Schweizer <sup>1</sup>, K. Spanaus <sup>3</sup>, L. P. Westphal <sup>1</sup>, C. Nakas <sup>4</sup> and K. Mira <sup>5</sup>

<sup>1</sup> University and University Hospital of Zurich, Switzerland

<sup>2</sup> University Hospital Zürich, Switzerland

<sup>3</sup> University Hospital Zurich, University of Zurich, Switzerland

<sup>4</sup> University of Thessaly, Greece

<sup>5</sup> University and University Hospital Basel; University and University Hospital of Zurich, Switzerland

**Aims:** Ischemic stroke (IS) is the leading cause of epilepsy in elderly patients. Blood biomarkers acquired in the acute phase may contribute to early prediction and risk stratification for post stroke epilepsy (PSE), thus identifying vulnerable patients that are most likely to benefit of antiepileptic treatment. Increased permeability of blood-brain barrier and neuro-inflammation are crucial in the process of epileptogenesis. Elevation of S100-B serum levels is a marker of cell damage, studies with murine models and with large collectives of human patients have been already proposed this protein as a prognostic biomarker for PSE. We aim to assess and validate the predictive value for PSE of S100-B using a large well characterized acute IS cohort.

**Methods:** Within the multicenter BIOSIGNAL (Biomarker Signature of Stroke Aetiology) study (ClinicalTrials.gov NCT02274727), we consecutively included 1161 ischemic stroke patients at the stroke center of the university hospital of Zurich 24 h of symptom onset. Clinical work-up during the hospitalization included medical history, physical examination, clinical risk scoring using NIHSS, routine laboratory tests & imaging (CT and /or MRI) and aetiology work up (ECG, Echocardiography, Ultrasound). Blinded S100-B measurement was performed within 24 h of symptom onset. The primary endpoint late seizure more than 7 days after stroke and secondary endpoint was any seizure, during a long follow up period (follow-up median duration 5 year, Q1 5 years, Q3 6 years). Logistic regression models were fitted to estimate odds ratio (OR) and 95% confidence interval (CI) for the association between log-S-100B and the outcome, while extreme gradient boosting techniques were used to assess optimal, predictive multivariable models.

**Results:** Among 1161 acute IS patients, 69 developed late seizure and 101 developed any seizure. After adjusting for demographic and vascular risk factors there was no significant

association between log-S100B levels neither with late nor with any seizure during the follow up. Machine learning approaches led to the same conclusions.

**Conclusions:** Despite previous pilot studies in this large cohort study we were not able to find a significant association between levels of S-100B and development of PSE. Other candidate biomarkers should be further evaluated for this important clinical question.

P041

### Central Retinal Artery Occlusion: Current Practice and Prehospital Delays in Switzerland

E. Ardila Jurado <sup>1</sup>, V. Sturm <sup>1</sup>, F. Brugger <sup>2</sup>, K. Nedeltchev <sup>3</sup>, M. Arnold <sup>4</sup>, L. Bonati <sup>5</sup>, E. Carrera <sup>6</sup>, P. Michel <sup>7</sup>, C. W. Cereda <sup>8</sup>, M. Bolognese <sup>9</sup>, S. Albert <sup>10</sup>, F. Medlin <sup>11</sup>, C. Berger <sup>12</sup>, L. Schelosky <sup>13</sup>, S. Renaud <sup>14</sup>, J. Niederhauser <sup>15</sup>, C. Bonvin <sup>16</sup>, M. Mono <sup>17</sup>, B. Rodic <sup>18</sup>, A. Tarnutzer <sup>19</sup>, G. Schwegler <sup>20</sup>, S. Salmen <sup>21</sup>, A. R. Luft <sup>22</sup>, N. Peters <sup>23</sup>, J. Vehoff <sup>24</sup> and G. Kägi <sup>2</sup>

<sup>1</sup> Kantonsspital St Gallen, Switzerland

<sup>2</sup> Kantonsspital St Gallen, Switzerland

<sup>3</sup> Aarau Cantonal Hospital, Switzerland

<sup>4</sup> Bern University Hospital, Switzerland

<sup>5</sup> University Hospital of Basel, Switzerland

<sup>6</sup> Geneva University Hospital, Switzerland

<sup>7</sup> Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland

<sup>8</sup> Lugano Regional Hospital, Switzerland

<sup>9</sup> Lucerne Cantonal Hospital, Switzerland

<sup>10</sup> Cantonal Hospital of Graubünden, Switzerland

<sup>11</sup> Fribourg Cantonal Hospital, Switzerland

<sup>12</sup> Hospital Sarganserland Grabs, Switzerland

<sup>13</sup> Kantonsspital Münsterlingen, Division of Neurology, Switzerland

<sup>14</sup> Cantonal Hospital Neuchâtel, Switzerland

<sup>15</sup> Groupement Hospitalier de l'Ouest Lémanique (GHOL), Switzerland

<sup>16</sup> Hôpital du Valais, Switzerland

<sup>17</sup> Triemli Hospital Zurich, Switzerland

<sup>18</sup> Kantonsspital Winterthur, Switzerland

<sup>19</sup> Kantonsspital Baden, Switzerland

<sup>20</sup> Spital Limmattal, Switzerland

<sup>21</sup> Centre Hospitalier Bienne, Switzerland

<sup>22</sup> University Hospital Zürich, Switzerland

<sup>23</sup> Clinic Hirslanden Zurich, Switzerland

<sup>24</sup> Kantonsspital St. Gallen, Switzerland

**Background:** CRAO is a serious condition leading to monocular blindness. Re-establishing retinal perfusion might prevent irreversible damage. Data about thrombolysis in CRAO are promising but good evidence is still lacking. Among others this is due to important prehospital delays. The aim of this study is to describe the current practice in patients with CRAO treated in Stroke Centers/Units (SCs/SUs) in Switzerland and the prehospital delays and pathways compared to patients with ischemic stroke based on the data from the Swiss Stroke Register (SSR)

**Methods:** We analysed registered cases with CRAO and ischemic stroke between January 2014 and December 2019. We describe and compare the prehospital pathways. Patients with CRAO were categorized into two groups: those receiving thrombolysis and those with standard of care treatment.

**Results:** 397 CRAO and 32,816 ischemic stroke cases were registered from 2014 until 2019 in 20 SC/ in Switzerland. The mean age was 71.8 (13.7) and 72.4 (13.7) years, respectively. Most of the CRAO Patients (41.0%) were referred from another hospital and had a lower rate of emergency referrals (5.9%). For CRAO-patients receiving thrombolysis, emergency referrals doubled (11.6%) at the expense of referrals from the GP (14.0%). Most of the CRAO patients (83.0%) used private transportation, and only 16.6% came by emergency

services. This contrast the number of stroke patients arriving at the hospital by the emergency services (65.3%). Hence, the symptom-to-door time was significantly longer in CRAO compared to stroke (852 min. vs. 300 min).

The thrombolysis rate was 13.2% for CRAO patients (8.9% systemic-and 4.3% intra-arterial thrombolysis), which is significantly lower than the observed thrombolysis rate in stroke patients (30.9%). Among CRAO patients with a symptom-to-door time of less than 4 h (26.0%), the thrombolysis rate was 45%. Of the remaining patients who arrived beyond 4 h after symptom onset, only 1,7% of the patients were thrombolysed.

**Conclusions:** The prehospital delays seems to be the main reason for withholding thrombolysis from patients with CRAO. Although CRAO is a serious condition affecting multiple aspects of daily living and the quality of life, specific prehospital pathways to improve symptom to door time are not defined. Reducing prehospital delays will increase thrombolysis rate and facilitate enrolment of patients in clinical trials in order to improve the poor outcome of CRAO

P042

### 10-Year Trends in Cardiovascular Risk Factors in Switzerland: Non-Traditional Risk Factors Are on the Rise in Women More than in Men

M. Hänsel <sup>1</sup>, K. Steigmiller <sup>2</sup>, A. R. Luft <sup>1</sup>, C. Gebhard <sup>3</sup>, U. Held <sup>2</sup> and S. Wegener <sup>1</sup>

<sup>1</sup> Department of Neurology and Clinical Neuroscience Center, University Hospital Zurich and University of Zurich, Switzerland

<sup>2</sup> Department of Biostatistics at Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Switzerland

<sup>3</sup> Department of Nuclear Medicine, University Hospital Zurich and University of Zurich, Switzerland

**Aims:** Effective control of cardiovascular risk factors is the prerequisite to prevent cardiovascular disease. It is increasingly clear that non-traditional cardiovascular risk factors (nt-cvrf) such as stress significantly add to cardiovascular risk arising from traditional cardiovascular risk factors (t-cvrf). To determine sex-specific changes and 10-year trends in prevalence of t-cvrf and nt-cvrf in Switzerland.

**Methods:** We obtained anonymized data from 22,134 participants (51% women) of the governmental Swiss Health Survey, performed every five years (2007, 2012, and 2017). Epidemiological parameters, t-cvrf and nt-cvrf were analyzed in a cross-sectional approach and observational study design. Temporal trends in epidemiological parameters, t-cvrf (e.g., hypertension, diabetes, hypercholesterolemia, alcohol/nicotine consumption, physical activity, smoking), and nt-cvrf (e.g., stress at work, feeling exhausted at work, working despite illness, locus of control, energy and vitality, sleep disorders, major depression) were matched by sex.

**Results:** Over the observation period, the number of women having full-time jobs increased considerably (2007: 38%, 2012: 39%, 2017: 44%). This was accompanied by a substantial rise in the prevalence of nt-cvrf including stress at work (2007: not available, 2012: 59%, 2017: 66%), reduced feeling of energy and vitality (2007: not available, 2012: 23%, 2017: 29%), and sleep disorders (2007: 26%, 2012: 24%, 2017: 29%) in women. This trend was less pronounced in men. Amongst t-cvrf, only the prevalence of obesity and hypercholesterolemia increased over time in both sexes, while other t-cvrf remained stable (hypertension [27%], diabetes [5%]) or decreased (smoking [9.4 cigarettes/day]).

**Conclusions:** A rise in women's economic participation alongside a pronounced increase in nt-cvrf in the female Swiss population emphasizes the need to improve cardiovascular risk stratification and implement effective preventive measures for neuro- and cardiovascular disease.



P043

### Lipoprotein (a) Is a Newly Validated Biomarker for Large Artery Atherosclerosis Stroke Aetiology

S. Rudin <sup>1</sup>, L. Kriemler <sup>2</sup>, T. Dittrich <sup>1</sup>, A. Zietz <sup>1</sup>, J. Schweizer <sup>3</sup>, M. Arnold <sup>3</sup>, P. Lyrer <sup>1</sup>, S. Engelter <sup>4</sup>, N. Peters <sup>5</sup>, F. Barinka <sup>5</sup>, S. Jung <sup>6</sup>, M. Arnold <sup>6</sup>, U. Fischer <sup>1</sup>, K. Rentsch <sup>7</sup>, M. Christ-Crain <sup>8</sup>, M. Katan <sup>1</sup> and G. M. De Marchis <sup>1</sup>

<sup>1</sup> Department of Neurology, University Hospital and University of Basel, Switzerland

<sup>2</sup> Department of Internal Medicine, Kantonsspital Schaffhausen, Switzerland

<sup>3</sup> Department of Neurology, University Hospital and University of Zurich, Switzerland

<sup>4</sup> Department of Neurology, University Hospital Basel and University of Basel and Neurology and Neurorehabilitation, University Department of Geriatric Medicine Felix Platter, Switzerland

<sup>5</sup> Department of Neurology and Stroke Center, Hirslanden Hospital Zurich, Switzerland

<sup>6</sup> Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Switzerland

<sup>7</sup> Department of Laboratory Medicine, University Hospital and University of Basel, Switzerland

<sup>8</sup> Department of Endocrinology, University Hospital and University of Basel, Switzerland

**Background and aims:** Lipoprotein (a) (Lp (a)) serum levels are mainly genetically determined and contribute to atherogenesis. High Lp (a) levels are associated with an increased cardiovascular morbidity. Recently, serum Lp (a) levels have been associated with large artery atherosclerosis stroke (LAAS) aetiology. We aimed to validate this association in an independent cohort.

**Methods:** We included acute ischemic stroke patients from a prospective cohort study from the University Hospital Bern (Inselspital), Switzerland. Lp (a) serum levels were measured in serum, drawn within 24 h after symptom onset. Stroke subtype was determined according to the TOAST classification. We assessed the association of Lp (a) with LAAS in univariate and multivariate analysis, adjusting for traditional LAAS risk factors.

**Results:** Overall, 746 patients were included, of which 105 had a LAA stroke (14%). Lp (a) was higher in patients with LAAS compared to patients with non-LAAS (23.0 nmol/l [IQR:9.8–80.0] versus 16.3 nmol/l [IQR:5.8–57.0],  $p = 0.01$ ). In univariate analysis, patients with LAAS were significantly more often men, suffered more often from Dyslipidaemia, Arterial Hypertension, Diabetes and had a higher BMI than patients with non-LAAS. In a multivariable logistic regression model, elevated Log 10(Lp(a)) was associated with LAAS with a OR of 1.50 (95%CI 1.02–2.21).

**Conclusions:** Among ischemic stroke patients, we could validate the independent association of higher Lp (a) levels with LAAS aetiology, also after adjusting for traditional cardiovascular risk factors. Independent validation of biomarkers, especially with the aim to guide secondary prevention, is essential. These findings are relevant in view of randomised clinical trials investigating the effect of specific Lp (a) lowering agents in reducing major adverse cardiovascular events.

P044

### Awareness of Central Retinal Artery Occlusion (CRAO) on the Population, General Practitioners and Ophthalmologist Level in Eastern Switzerland

E. Ardila Jurado, V. Sturm, F. Brugger, J. Vehoff and G. Kägi

Kantonsspital St Gallen, Switzerland

**Background:** CRAO is a serious condition leading to monocular blindness. Re-establishing retinal perfusion might prevent irreversible damage. Data about thrombolysis in CRAO are promising but good evidence is still lacking. Among others this is due to important prehospital delays. The aim of this study was to assess the level

of awareness of CRAO symptoms and handling of these patients amongst the general population, general practitioners (GPs) and ophthalmologists in Eastern Switzerland.

**Methods:** The survey was carried out between March 2019 and July 2020. The population-level was assessed with an 16 questions questionnaire about demographic data, recognition of CRAO warning signs, underlying causes, and approach in case of acute unilateral visual loss as well as in case of stroke symptoms. GPs and ophthalmologist filled out an online 16 and 11 questions questionnaire, respectively, regarding symptoms of CRAO, differential diagnosis, etiology, approach in case of persistent and temporary acute visual loss, therapy options, and time windows.

**Results:** 350 people participated in the population survey. 28.6% identified an unilateral, sudden loss of vision as a symptom of CRAO. CRAO was considered a medical emergency by 63.1% of them. 55.4% would go to the hospital in case of acute visual loss compared to 89.9% with stroke symptoms. 69.7% identified a temporary visual loss as potentially harmful and would consult a doctor.

66 of 67 (98.5%) surveyed ophthalmologists recognise CRAO as a medical emergency, and 64.2% of them would transfer their patients to a stroke center. Only 23.9% would consider systemic thrombolysis and 41.8% intra-arterial thrombolysis as a beneficial therapy. All GPs (102) recognise CRAO as an emergency and 88.2% recognised a sudden unilateral loss of vision as the typical symptom in CRAO. 59.8% of them would transfer the patient to the next stroke center. 55.3% and 37.3% consider intra-arterial and systemic thrombolysis respectively as potentially effective.

**Conclusions:** Awareness on population level of symptoms and urgency of CRAO is rather low in Eastern Switzerland. Although the symptoms recognition among GPs and ophthalmologist is good the acceptance of thrombolysis as a possible treatment option is low. Current delays in the prehospital phase in case of CRAO represent the main obstacle for reperfusion therapies/studies. Information campaigns are needed to benefit from the existing prehospital organizational models for stroke.

P045

### Mechanical Thrombectomy versus Best Medical Treatment in Late Window Large Vessel Occlusion Patients Who Do Not Fulfill the Defuse-3 and Dawn Criteria

T. D. Dittrich <sup>1</sup>, P. Sporns <sup>2</sup>, L. Kriemler <sup>3</sup>, S. Rudin <sup>4</sup>, A. Nguyen <sup>5</sup>, A. Zietz <sup>4</sup>, A. Polymeris <sup>4</sup>, C. Tränka <sup>4</sup>, S. Thilemann <sup>4</sup>, B. Wagner <sup>4</sup>, V. Altersberger <sup>4</sup>, I. Piot <sup>4</sup>, F. Barinka <sup>6</sup>, S. Müller <sup>7</sup>, M. Hänsel <sup>8</sup>, H. Gensicke <sup>9</sup>, S. Engelter <sup>9</sup>, P. Lyrer <sup>4</sup>, R. Sutter <sup>10</sup>, C. Nickel <sup>11</sup>, M. Katan <sup>12</sup>, N. Peters <sup>13</sup>, Z. Kulcsár <sup>7</sup>, G. Karwacki <sup>14</sup>, M. Pileggi <sup>15</sup>, C. Cereda <sup>16</sup>, S. Wegener <sup>8</sup>, L. Bonati <sup>17</sup>, U. Fischer <sup>4</sup>, M. Psychogios <sup>5</sup> and G. M. De Marchis <sup>4</sup>

<sup>1</sup> University Hospital Basel and University of Basel, Switzerland

<sup>2</sup> Department of Neuroradiology, University Hospital Basel, Basel, Switzerland and Department of Diagnostic and Interventional Neuroradiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

<sup>3</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland and Clinic for Internal Medicine, Cantonal Hospital Schaffhausen, Schaffhausen, Switzerland

<sup>4</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>5</sup> Department of Neuroradiology, University Hospital Basel, Basel, Switzerland

<sup>6</sup> Department of Neurology and Stroke Center, Hirslanden Hospital Zurich, Zurich, Switzerland

<sup>7</sup> Department of Neuroradiology, University Hospital Zurich, Zurich, Switzerland

<sup>8</sup> Department of Neurology, University Hospital Zurich and University of Zurich, Zurich, Switzerland

<sup>9</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland and Neurology and Neurorehabilitation, University Department of Geriatric Medicine Felix Platter, Basel, Switzerland

<sup>10</sup> Department of Intensive Care Medicine, University Hospital Basel, Basel, Switzerland

<sup>11</sup> Emergency Department University Hospital Basel and University of Basel, Basel, Switzerland

<sup>12</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland and Department of Neurology, University Hospital Zurich and University of Zurich, Zurich, Switzerland

<sup>13</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland and Department of Neurology and Stroke Center, Hirslanden Hospital Zurich, Zurich, Switzerland

<sup>14</sup> Department of Radiology and Nuclear Medicine, Cantonal Hospital of Lucerne, Lucerne, Switzerland

<sup>15</sup> Department of Neuroradiology, EOC Neurocenter of Southern Switzerland, Lugano, Switzerland

<sup>16</sup> Department of Neurology and Stroke Center, EOC Neurocenter of Southern Switzerland, Lugano, Switzerland

<sup>17</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland and Rheinfelden Rehabilitation Clinic, Rheinfelden, Switzerland

**Background:** We assessed the efficacy and safety of mechanical thrombectomy (MT) in adult stroke patients with anterior circulation large vessel occlusion (LVO) presenting in the late window who did not fulfill the DEFUSE-3 and DAWN inclusion criteria.

**Methods:** Cohort study of adults with LVO admitted between 6 and 24 h after last seen well at five participating Swiss Stroke Centers between 2014 and 2021. Mismatch was assessed by CT or MRI perfusion with an automated software (RAPID or OLEA). We excluded patients meeting DEFUSE-3 and DAWN inclusion criteria and compared those who underwent MT with those receiving best medical treatment alone (BMT) by inverse probability of treatment weighting (IPTW) using the propensity score. The primary efficacy endpoint was a favorable functional outcome at 90 days, defined as a modified Rankin Scale (mRS) score of 0–2, or a mRS shift toward lower categories. The primary safety endpoint was symptomatic intracranial hemorrhage (sICH).

**Results:** Among 278 patients with LVO presenting in the late window, 190 (68%) did not meet the DEFUSE-3 and DAWN inclusion criteria and thus were included in the analyses. Of those, 102 (54%) received MT. In the IPTW analysis, patients in the MT group had higher odds of favorable outcomes compared to the BMT group (mRS 0–2: aOR 1.57 [1.02–2.44],  $p = 0.04$ , mRS shift: cOR 0.68 [0.47–0.99],  $p = 0.045$ ). There were no significant differences in sICH (MT vs. BMT: 5% vs. 2%,  $p = 0.63$ ) or all-cause death within 90 days (aOR 0.68 [0.43–1.08],  $p = 0.10$ ).

**Conclusions:** Two out of three patients with LVO presenting in the late window did not meet the DEFUSE-3 and DAWN inclusion criteria. In these patients, MT was associated with higher odds of favorable functional outcomes without increased rates of sICH. These findings support the enrolment of patients into ongoing randomized trials on MT in the late window with more permissive inclusion criteria.

P046

## Early Origin of Mental Health: Maternal Adverse Childhood Events Increase Risk of Postpartum Depression and Impaired Bonding

K. Probst <sup>1</sup>, S. Tschudin <sup>2</sup>, I. Hoesli <sup>2</sup>, S. Brand <sup>3</sup>, M. Hatzinger <sup>1</sup> and T. Mikoteit <sup>1</sup>

<sup>1</sup> Psychiatric Services Solothurn, Switzerland

<sup>2</sup> University of Basel/ University Hospital of Basel, Switzerland

<sup>3</sup> University Psychiatric Clinics of Basel, Switzerland

**Aims:** Adverse childhood events (ACE) such as maltreatment or neglect during childhood can have an imprinting effect on child development and adult mental health. It is assumed that early programming of the stress response system is a mediating factor between ACE and later stress associated disorders like depression. In addition, ACE may have an impact on bonding style. The aim of this study was to examine, whether maternal ACE have an impact on the risk for postpartum depression and the quality of mother-infant bonding. And if so, whether hypothalamus-pituitary-adrenal (HPA) axis activity as reflected by hair steroids were involved in this association.

**Methods:** Thirty-six pregnant women ( $M = 33.3$  years,  $SD = 4.4$ ) were recruited in an outpatient setting. At study inclusion (before 32 weeks gestation), ACE were assessed with the Childhood Trauma Questionnaire Short Form (CTQ-SF). At 12 weeks postpartum, levels of hair cortisol and hair cortisone, degrees of depression (HAMD, EPDS), anxiety

(STAI), insomnia (ISI), perceived stress (PSS, PSI), and impairment of mother-infant bonding (PBQ) were assessed.

**Results:** Inconsistency experiences during maternal childhood correlated positively with impaired bonding ( $r = 0.646$ ,  $p = 0.002$ ), rejection and anger to the child ( $r = 0.632$ ,  $p = 0.002$ ), and anxiety about caring for the child ( $r = 0.538$ ,  $p = 0.012$ ). Moreover inconsistency experiences were related to higher scores of depression ( $r = 0.690$ ,  $p < 0.001$ ) at 12 weeks postpartum. Furthermore, impaired bonding ( $r = 0.631$ ,  $p = 0.003$ ) and anxiety about caregiving ( $r = 0.538$ ,  $p = 0.012$ ) positively influenced the association between inconsistency experiences and postpartum depression. Further, no significant association was shown between cortisol ( $r = 0.310$ ,  $p = 0.242$ ) or cortisone ( $r = 0.477$ ,  $p = 0.061$ ) and inconsistency experiences. However, hair cortisol ( $r = 0.750$ ,  $p = 0.001$ ) as well as hair cortisone ( $r = 0.701$ ,  $p = 0.004$ ) positively influenced the association between inconsistency experiences and postpartum depression.

**Conclusions:** Inconsistency experiences in childhood were related to both, impaired mother-infant bonding as well as a higher risk of postpartum depression. Furthermore, the magnitude of the association between inconsistency experiences and postpartum depression was influenced by both, poor bonding as well as by increased levels of hair cortisol and cortisone, which indicate an increased HPA activity.

P047

### Hair Cortisol and Cellular Aging: Associations of Chronic Hypothalamic Pituitary Adrenal Axis Activation and Telomere Length in a High-Risk Sample of Young Adults

N. Varghese<sup>1</sup>, D. Bürgin<sup>2</sup>, V. Clemens<sup>3</sup>, C. Boonmann<sup>2</sup>, E. Unternährer<sup>2</sup>, A. O'Donovan<sup>4</sup>, M. Schmid<sup>2</sup> and A. Eckert<sup>1</sup>

<sup>1</sup> University of Basel, Basel, Switzerland, Neurobiology Lab for Brain Aging and Mental Health, Transfaculty Research Platform Molecular & Cognitive Neuroscience, Switzerland

<sup>2</sup> Psychiatric University Hospitals, Child and Adolescent Psychiatric Research Department (UPKKJ), University of Basel, Basel, Switzerland

<sup>3</sup> University Hospital Ulm, Germany

<sup>4</sup> Department of Psychiatry and Weill Institute for Neurosciences, University of California San Francisco, San Francisco, USA

**Aim:** High experienced stress correlates to accelerated biological aging and adverse health outcome. As an aging indexer, shortening leukocyte telomere length (LTL) may be associated to activating the hypothalamic-pituitary-adrenal (HPA) axis putative to stress. Hair cortisol concentration (HCC) has risen to be a standard of the HPA axis activation. Due to a lack of biological measures of chronic biological stress, the investigation between long-term stress and cellular aging has been challenging. This study aimed to assess the association between HCC and LTL of young adults to examine the relationship between chronic biological stress and LTL in the content of aging.

**Methods:** This study was conducted in a highly strained, at-risk sample of young adults with previous residential child welfare placement. The study size consisted of 92 participants (38% women and 62% men). For the Cortisol measurement, 2 cm of hair was utilised (approx. eight weeks of cortisol excretion). LTL was assessed with quantitative PCR in whole blood samples. Polynomial and linear regression were used for the correlation analysis between LTL and HCC.

**Results:** Between HCC and LTL a negative correlation ( $\rho/r = -0.68$ ,  $p < 0.001$ ) was found indicating that higher HCCs are linked to shorter LTL. HCC explained about 50% of the variance to LTL. A curvilinear relationship showed a strong negative association with lower cortisol concentration (0–10 pg/mg). Still, the analysis demonstrated no correlation at higher cortisol levels (>10 pg/mL) in the polynomial regression models.

**Conclusions:** This study is the first to examine the correlation between HCCs and LTL. This study demonstrated that higher HCCs were associated with a shorter LTL in humans,

thereby potentially involving the HPA axis by prolonged cortisol secretion to telomere length. Consequently, HCC might be a potential indicator for investigating chronic stress linked with aging-related processes. Further clarification of this association, a more extensive and diverse sample is needed.

P048

### Oral Prolonged-Release Ketamine in Treatment-Resistant Depression—A Double-Blind Randomized Placebo-Controlled Multicentre Trial of KET01, a Novel Ketamine Formulation

B. Offenhammer <sup>1</sup>, M. Colla <sup>1</sup>, G. Kronenberg <sup>1</sup>, J. Mutschler <sup>2</sup>, T. Mikoteit <sup>3</sup>, C. Eicher <sup>1</sup>, S. Vetter <sup>1</sup>, H. Scheerer <sup>1</sup>, A. B. Bruehl <sup>4</sup> and E. Seifritz <sup>1</sup>

<sup>1</sup> Department of Psychiatry, Psychotherapy and Psychosomatics; Psychiatric University Hospital Zurich; University of Zurich, Switzerland

<sup>2</sup> Psychiatric Hospital Meiringen, Switzerland

<sup>3</sup> Psychiatric Services Solothurn and Department of Medicine, University of Basel, Switzerland

<sup>4</sup> University Psychiatric Clinics Basel, University of Basel, Switzerland

**Background:** Ketamine holds great promise for the treatment of patients suffering from treatment-resistant depression (TRD) and is usually administered intravenously or intranasally. [1],[2],[3] Here, we investigated the antidepressant effects of a novel prolonged-release formulation of racemic ketamine (KET01) taken orally.

**Methods:** We included inpatients who had failed to respond to at least two adequate antidepressant treatment courses for the current depressive episode. The participants received either 160 mg/d or 240 mg/d BID of oral prolonged-release ketamine or placebo for 14 days as an add-on treatment. The primary endpoint was defined as the change in Montgomery-Asberg Depression Rating Scale (MADRS) scores from baseline to day 15. We used analyses of variance followed by pairwise least-squares mean difference tests in a mixed model repeated measures. The study was conducted at three large Swiss psychiatric hospitals. The trial was approved by the local ethics committee and pre-registered with the Swiss National Clinical Trials Portal.

**Results:** Of the 30 patients enrolled in this study, 27 completed double-blind treatment and were included in the analyses (160 mg/d: n = 7, 240 mg/d: n = 10, placebo: n = 10). The study was discontinued prematurely, mostly due to problems with recruitment in the context of the COVID-19 pandemic. The mean (SD) baseline MADRS score was 31 (5.88). Mean MADRS scores on day 15 were 17 (240 mg/d), 25 (160 mg/d), and 23 (placebo). The mean change in MADRS score observed on day 15 in the 240 mg/d group was larger than in the placebo group with −4.99 (95% CI: −11.81, 1.83,  $p = 0.15$ ) and 1.39 in the 160 mg/d group (95% CI: −6.06, 8.83,  $p = 0.71$ ). Additionally, the data suggests a rapid onset of action in the 240 mg/d group and good tolerability with no treatment-related serious adverse events, no clinically relevant effects on blood pressure or on dissociation.

**Conclusions:** Based on the primary endpoint clinical data reported here, a positive trend of antidepressant efficacy is evident in this study. The add-on oral administration of prolonged-release ketamine at a dosage of 240 mg/d may be promising for the treatment of treatment-resistant depression. Given the ease of application and relatively few side effects, this route of ketamine administration may, in certain instances, offer advantages over other modes of ketamine administration. More research is required to confirm the antidepressant effect of KET01.

P049

### The Origins of the Dark–High Externalizing Problems, High Hyperactivity, and Low Prosocial Behavior at Age 5 Are Correlated with More Callousness and Lower Empathy at Age 14

L. Eisenhut <sup>1</sup>, D. Sadeghi-Bahmani <sup>2</sup>, V. T. Ngo <sup>1</sup>, A. Brühl <sup>1</sup>, T. Mikoteit <sup>3</sup>, M. Hatzinger <sup>3</sup> and S. Brand <sup>1</sup>

<sup>1</sup> Psychiatric Hospital of the University of Basel, Switzerland

<sup>2</sup> Stanford University, Department of Psychology, USA

<sup>3</sup> Psychiatric Hospital of Solothurn, Switzerland

**Background:** Adolescents with externalizing behavioral issues such as aggressive behavior and callous-unemotional traits pose a challenge both for their individual psychosocial development and for the society. By contrast, traits of empathy might counterbalance adverse behavior. Further, there is some, but inconsistent research as regards the predictive value of objective sleep parameters for future psychological functioning. We addressed this issue and asked, if and to what extent longitudinally behavior and objective sleep at the age of five years could predict dimensions of callous-unemotional behavior and empathy. Cross-sectionally, we asked, if subjective sleep and stress were associated with callous-unemotional behavior and empathy.

**Methods:** At total of 80 preschoolers (mean age: five years) underwent objective sleep-EEG recordings. Their parents completed the Strengths and Difficulties Questionnaire (SDQ). At the age of 14 years, that is, nine years later, participants completed a series of self-rating questionnaires on callous-unemotional behavior, empathy, subjective sleep, and stress perception.

**Results:** Cross-sectionally, higher scores for insomnia were associated with higher scores for callous-unemotional behavior, and lower scores for empathy. Higher stress scores were associated with higher callous-unemotional behavior. Longitudinally, at the age of five years, lower sleep-EEG-assessed sleep efficiency indices, a longer sleep-onset latency and a shorter sleep duration predicted higher scores for callous-unemotional behavior at the age of 14 years. Further, At the age of five years, higher externalizing problems and higher hyperactivity scores predicted higher scores for callous-unemotional behavior. At the age of five years, higher negative peer relations and lower prosocial behavior predicted lower scores for empathy at the age of 14 years.

**Conclusions:** Data suggest that objectively measured sleep indices and behavioral issues, as rated by parents, at preschool age have the power to predict dimensions of emotion regulation at the age of 14 years. Current subjective sleep quality and stress may confound or intensify these patterns of association.

P050

### 2D:4D-Ratio Was Associated with Higher Sociosexual Orientation, but Not with Current Physical Activity Pattern—Results from a Sample with Young Adults

D. Sadeghi-Bahmani <sup>1</sup>, D. Kalt <sup>2</sup>, M. Gerber <sup>2</sup>, A. Brühl <sup>3</sup>, K. Dürsteler <sup>3</sup> and S. Brand <sup>3</sup>

<sup>1</sup> Stanford University, USA

<sup>2</sup> University of Basel, Basel, Switzerland

<sup>3</sup> Psychiatric Hospital of the University of Basel, Switzerland

**Background:** Individuals scoring high in Dark Triad traits (psychopathy, narcissism, Machiavellianism) also report higher scores on sociosexual orientation. Further, among successful professional athletes, physical activity performance was associated to a lower 2D:4D-ratio: the length of the index finger is shorter compared to the length of the ring finger; this is understood as a proxy of increased perinatal exposure to testosterone. Here,

we investigated the associations between Dark Triad traits, 2D:4D-ratio, sociosexual orientation, and current and past physical activity patterns among a sample of young non-athlete adults.

**Method:** A total of 90 adults (mean age: 23 years; 55.2% males) took part in this study. They completed a series of self-rating questionnaires covering demographic information, Dark Triad traits, sociosexual orientation, and current and past physical activity patterns. Further, participants provided a scan of the palm of their right hand.

**Results:** Compared to female participants, male participants had a lower 2D:4D-ratio and reported higher scores on sociosexual orientation. A lower 2D:4D-ratio was associated with higher current and past physical activity patterns. While the current physical activity pattern was associated with higher Dark Triad traits, higher past physical activity patterns were associated with lower Dark Triad traits. Higher current physical activity patterns were associated with a higher sociosexual orientation, male gender and higher Dark Triad scores,

**Conclusions:** The current pattern of results suggests that individuals prenatally exposed to higher testosterone concentrations might benefit from this programmed physiological pattern, once they are adults.

P051

### The Sweet Spot for Sweet Sport. Costs and Benefits and Non-Linear Associations between Mental Health and Daily Sports Activity in a Sample of Young Adults

S. Bur <sup>1</sup>, L. Eisenhut <sup>2</sup>, K. Dürsteler <sup>2</sup> and S. Brand <sup>2</sup>

<sup>1</sup> University of Basel, Basel, Switzerland

<sup>2</sup> Psychiatric Hospital of the University of Basel, Switzerland

**Background:** Nowadays, physical inactivity is a global health problem and negatively associated with physical and mental health. In contrast, excessive training is also associated with physical and mental risks. We tested the hypothesis that there is a so-called „sweet spot“. “Sweet spot” refers to an optimal amount of sports activity in which mental health reaches an optimal level. In a second hypothesis, it was assumed that people who are very active in sports must compromise on more things than people who do less sports. Research should also be carried out into the main things these people have to renounce.

**Methods:** A total of 197 people (average age: 28 years; 64% women) participated in the online survey. Participants answered questions regarding the use of their daily time budget, motivation for exercising, mental health, and the sacrifices they must make because of exercising. They were divided into five categories: category 0 (<1 h sport/day), category 1 (1 h sport/day), category 2 (2 h sport/day), category 3 (3 h sport/day), and category 4 (≥4 h sport/day).

**Results:** Mental health indices increased to a “sweet point” of 2–3 h/d, while a higher amount of daily exercising (4+ h/d) was associated with more health issues. In the group of +4 h/d, time budget was shortened to keeping social contacts with family members, peers and peers at work. Importantly, very high exercisers rated the decrease of social contacts as particularly unpleasant.

**Conclusions:** The patterns of results suggests that the “sweet point” is about 2–3 h of daily physical activity and exercising. A higher duration and intensity of physical activity and exercising is related to shortened time budget for keeping social contacts with family members, and peers. Importantly, the relative lack of social contacts was understood as particularly unpleasant.

P052

### Emotional Competencies in Multiple Sclerosis

D. Sadeghi Bahmani <sup>1</sup>, L. S. Bahmani <sup>2</sup>, O. Mirmosayyeb <sup>3</sup>, V. Shaygannejad <sup>3</sup> and J. J. Gross <sup>1</sup>

<sup>1</sup> Stanford University, USA

<sup>2</sup> Shahid Ashrafi Esfahani University, Iran

<sup>3</sup> Isfahan university of medical science, Iran

**Background:** Emotional competencies are understood as the appropriate management of one's own emotions. As such, emotional competencies are also crucial for successful social interactions. However, among individuals with multiple sclerosis (MS), emotional competencies have not been investigated. Given this, the first aim of the present study was to compare the scores for emotional competencies between individuals with MS, adults of the general population, and adults with major depressive disorder. The second aim was to investigate the association of emotional competencies with MS-related symptoms of insomnia, depression, fatigue, and paresthesia. The third aim was to identify possible predictors of emotional competencies, including intolerance of uncertainty and mental toughness.

**Methods:** A total of 1135 individuals with MS (mean age: 34.56 years; 74.32% females; median EDSS: 2, range: 0–5) completed a series of self-rating questionnaires covering sociodemographic and MS-related information, emotional competencies, insomnia, depression, fatigue, paresthesia, and intolerance of uncertainty and mental toughness. Participants' emotional competencies were compared with adults of general population and major depressive disorder.

**Results:** Compared to general population, individuals with MS reported worse emotional competencies (small to large effect sizes). Compared to individuals with major depressive disorders, individuals with MS reported similar scores (trivial to small effect sizes). Higher scores for emotional competencies were associated with lower symptoms of insomnia, depression, fatigue, paresthesia, and intolerance of uncertainty, and with higher scores for mental toughness. Lower scores for depression and higher scores for mental toughness predicted higher emotional competencies. Higher scores for mental toughness statistically moderated associations between higher scores for depression and lower scores for emotional competencies.

**Conclusions:** Individuals with MS scored low in emotional competencies, and such scores were related with a broad range of MS-related symptoms, including intolerance of uncertainty. Mental toughness appeared to counterbalance the association between low emotional competencies and symptoms of depression. As such, it is conceivable that specific psychotherapeutic interventions may improve emotional competencies via improved mental toughness and decreased symptoms of depression.

P053-YouClin

### Effects of Acceptance and Commitment Therapy (ACT) and Mindfulness-Based Stress Reduction (MBSR) on Symptoms and Emotional Competencies in Individuals with Multiple Sclerosis

D. Sadeghi Bahmani <sup>1</sup>, L. Esmaeili <sup>2</sup>, F. Mokhtari <sup>3</sup>, L. S. Bahmani <sup>2</sup>, M. Afsharzadeh <sup>3</sup>, V. Shaygannejad <sup>3</sup>, O. Mirmosayyeb <sup>3</sup> and J. J. Gross <sup>1</sup>

<sup>1</sup> Stanford University, USA

<sup>2</sup> Shahid Ashrafi Esfahani University, Iran

<sup>3</sup> Isfahan university of medical science, Iran



**Background:** Compared to the general population, individuals with multiple sclerosis (MS) report higher levels of insomnia, depression, fatigue, and paresthesia, and lower levels of emotional competencies (understanding emotions in self and others). Available treatments are limited, and novel approaches to reducing symptoms and enhancing emotional competencies in MS are needed. Two potentially beneficial treatments are Acceptance and Commitment Therapy (ACT) and Mindfulness-Based Stress Reduction (MBSR). The aim of the present study was to investigate the impact of ACT and MBSR on symptoms and emotional competencies in patients with MS.

**Methods:** A total of 76 individuals with MS (81.6% females; mean age: 38.88 years; EDSS median: 2, range: 0–5) were randomly assigned to an 8-week ACT treatment, an 8-week MBSR treatment, or a wait-list control condition. At baseline and study-end (week 8), participants completed a series of questionnaires covering symptoms and emotional competencies. At mid-term (week 4), participants rated their insomnia and depression.

**Results:** Over time, symptoms of MS decreased and emotional competencies improved, but more so in the MBSR and ACT conditions, compared with the control condition. At study-end, the outcome improvement did not differ between the ACT and MBSR conditions.

**Conclusions:** Both ACT and MBSR led to reduced symptoms and enhanced emotional competencies. Psychotherapeutic interventions such as these should be considered as a means of decreasing symptoms and increasing emotional competencies among individuals with MS.

P054

### The Adaptive Cognitive Evaluation (ACE-X)—A Tablet Video Game for the Screening of Executive Deficits after Stroke

E. Fischer <sup>1</sup>, R. Schumacher <sup>1</sup>, A. Manuel Stocker <sup>2</sup>, P. Grivaz <sup>2</sup>, P. Götschmann <sup>1</sup>, A. Guggisberg <sup>1</sup>, M. Arnold <sup>1</sup>, T. Nef <sup>3</sup>, J. Younger <sup>4</sup>, J. Anguera <sup>4</sup>, A. Gazzaley <sup>4</sup>, P. Ryvlin <sup>5</sup>, R. Müri <sup>1</sup> and A. Sokolov <sup>2</sup>

<sup>1</sup> Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Switzerland

<sup>2</sup> Neuroscape@NeuroTech, Service de neuropsychologie et de neuroréhabilitation, Département des neurosciences cliniques, CHUV, University Hospital Lausanne, Switzerland

<sup>3</sup> Gerontechnology and Rehabilitation Group, Artificial Organ Center for Biomedical Engineering Research (ARTORG), University of Bern, Switzerland

<sup>4</sup> Neuroscape Center, Weill Institute of Neuroscience, Department of Neurology, University of California San Francisco, USA

<sup>5</sup> Department of Clinical Neurosciences, CHUV, Lausanne University Hospital, Switzerland

**Aims:** Stroke is among the leading causes of disability in adults, (1) with over 15,000 new cases per year in Switzerland alone. Around 30% of stroke patients suffer from deficits in executive function, a series of high-order cognitive processes vital for adaptive goal-directed behavior. (2) These deficits often persist in the long-term (3) and interfere significantly with everyday life. (4) Diagnosis of executive deficits requires extensive testing by trained neuropsychologists or cognitive neurologists. However, rather precise screening would be useful to assess the need for and orient the neuropsychological examination. The aim of this study is to assess the validity of a tablet-based and gamified battery Adaptive Cognitive Evaluation (ACE-X) for the screening of executive deficits after stroke.

**Methods:** In this cross-sectional study, we included 31 inpatients with unilateral ischemic or hemorrhagic stroke from two neurorehabilitation units at the University Hospital Inselspital Bern, Switzerland. Exclusion criteria were the inability to engage in the tablet-based assessment due to insufficient vision, central visual field, visuospatial attention, comprehension of instructions or distal upper extremity strength. After giving consent, patients underwent ACE-X testing including reaction time, visuospatial working

memory, multitasking, cognitive flexibility and cognitive interference. The results were correlated to corresponding neuropsychological tests routinely performed in inpatient neurorehabilitation.

**Results:** The mean age at inclusion was 58.6 years, 10 patients were female. 87% (n = 27) of patients suffered an ischemic stroke and 58% (n = 18) presented with a right hemispheric lesion. Strong and significant correlations of ACE-X and corresponding neuropsychological tests were found for reaction time, multitasking and cognitive flexibility, while a trend was observed in the correlations for cognitive interference. No significant correlation was detected between the visuospatial working memory tasks.

**Conclusions:** The tablet-based closed-loop adaptive video game ACE-X may represent a valid screening battery for executive dysfunction in stroke patients. The motivating video game setting including real-time adaptation and feedback is an unusual yet promising context for cognitive assessment, providing the opportunity for remote screening, also in other neurological and psychiatric conditions such as multiple sclerosis, dementia or schizophrenia.

P055

### Insomnia and Depression among Individuals with Multiple Sclerosis before and during the COVID-19—Results from a Prospective Longitudinal Study

D. Sadeghi Bahmani <sup>1</sup>, Y. Mohammadian <sup>2</sup>, L. S. Bahmani <sup>3</sup>, N. Piri <sup>2</sup>, H. Khazaie <sup>2</sup> and J. J. Gross <sup>1</sup>

<sup>1</sup> Stanford University, USA

<sup>2</sup> Kermanshah University of Medical Sciences, Iran

<sup>3</sup> Shahid Ashrafi Esfahani University, Iran

**Introduction:** There is some -- but inconsistent -- evidence that sleep and psychological health have deteriorated in the general population as a result of the COVID-19-pandemic and its related social restrictions. In the present study, we investigated whether and to what extent symptoms of insomnia, depression, fatigue, and paresthesia changed from before to during the COVID-19-pandemic among women diagnosed with multiple sclerosis (MS).

**Methods:** A total of 90 women with MS (mean age; 37.62 (SD = 8.61) years; EDSS score: median: 2.5 (range: 0–6.50)) completed a series of self-rating scales at two time points: Nine months before the COVID-19-outbreak in May 2019 (baseline) and during the COVID-19-pandemic (study end; 12 months after baseline: May 2020). Self-rating questionnaires covered sociodemographic and disease-related information, symptoms of insomnia, depression, fatigue, and paresthesia.

**Results:** Symptoms of depression increased over time (medium effect size: Cohen's d = 0.53), while symptoms of insomnia (small effect size: Cohen's d = 0.43), fatigue (trivial effect size: Cohen's d = 0.19), and paresthesia (trivial effect size: Cohen's d = 0.08) did not. The only predictor for insomnia during the COVID-19-pandemic was insomnia before the COVID-19-pandemic ( $\beta = 0.36$ ,  $p = 0.001$ ); the only predictor for depression during the COVID-19-pandemic was insomnia before the COVID-19-pandemic ( $\beta = 0.66$ ,  $p = 0.001$ );.

**Conclusions:** Overall, among a sample of female individuals with MS the COVID-19-pandemic and its related social restrictions may have had a modest influence on participants' core concerns of insomnia, depression, fatigue, and paresthesia.

P058

### High Frequency and Intensive Prevention Program for Cognitive Stabilization in Parkinson's Disease Patients

K. Toloraia, A. Meyer, M. Malaquini Stamato, U. Gschwandtner, P. Fuhr

Universitätsspital Basel, Switzerland

**Aims:** Cognitive decline is an important and common complication in Parkinson's disease (PD) patients since it significantly reduces the quality of life. A breakthrough in the treatment and prevention of cognitive decline in PD remains to be achieved. The individualized and intensive training programs applied here may prevent cognitive decline and improve quality of life.

**Methods:** Initially, 23 patients diagnosed with idiopathic PD (according to UK Parkinson's disease brain bank) completed a comprehensive neuropsychological test battery covering five domains (attention and working memory; verbal fluency and language; memory; executive functions; visuospatial functions) and were neurologically examined. The patients of the intervention group  $n = 15$  (4f;  $M = 63$  y; 59 y–75 y) underwent twice-weekly sessions of Tai Chi therapy over 4 weeks. PD patients also carried out an individually tailored training program consisting of two modules (smartphone-based speech and cognitive training). The frequency and duration of the training modules were modular and adapted to the initially measured severity of cognitive and speech deficits between 2 up to 5 sessions per week.

A matched control group (age, sex, education, disease duration) consisted of  $n = 8$  PD patients (1f,  $M = 68$  y; 62 y–72 y) who received an unspecific health enhancement program for nine weeks. Data were analysed with repeated-measures ANOVA.

**Results:** Four weeks of high-frequency training showed significant effects within group on visual episodic memory ( $[p = 0.046; \eta^2 = 0.255]$ ) and Rey-Osterrieth Complex Figure Test, immediate recall and delayed recall ( $[p < 0.001; \eta^2 = 0.615]$ ,  $[p = 0.004; \eta^2 = 0.466]$ ). Compared to the control group, the cognitive performance of the intervention group improved significantly in visual episodic memory ( $[p = 0.027, \eta^2 = 0.212]$ ); this significant difference was preserved after 6 months of follow-up ( $[p = 0.021; \eta^2 = 0.229]$ ).

**Conclusions:** High frequency and intensive prevention program shows good acceptance and feasibility in PD patients and has a relatively low dropout rate. An individually tailored training program might effectively improve cognitive deficits in patients with PD in visual episodic memory.

P059

### European Inter-Societal Delphi Consensus for the Biomarker-Based Etiological Diagnosis of Neurocognitive Disorders

V. Garibotto <sup>1</sup>, S. Morbelli <sup>2</sup>, C. Festari <sup>3</sup>, F. Massa <sup>4</sup>, M. Cotta Ramusino <sup>5</sup>, F. Nobili <sup>4</sup> and V. Frisoni <sup>6</sup>

<sup>1</sup> Geneva University Hospitals and Geneva University, Switzerland

<sup>2</sup> Genoa University Hospital, Italy

<sup>3</sup> IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Italy

<sup>4</sup> University of Genoa, Italy

<sup>5</sup> IRCCS Mondino Foundation, Italy

<sup>6</sup> University Hospitals of Geneva, Switzerland

**Aims:** Cerebrospinal fluid (CSF) and imaging biomarkers are necessary for the aetiological diagnosis of neurocognitive disorders, but evidence on their rational use in the clinic is incomplete. Since November 2020, a European multidisciplinary task force of

22 experts from eleven relevant scientific societies has defined a diagnostic workflow for the efficient use of biomarkers, filling the evidence gap on biomarker prioritisation with a formal Delphi consensus procedure. This abstract reports the preliminary results as of April 2022.

**Methods:** A modified Delphi method was used to create consensus. Group members participated in virtual Delphi rounds and voted on specific questions regarding the diagnostic workup of neurocognitive patients, based on their experience and evidence from the literature. Consensus was reached at a threshold of 70% agreement, or 50% + 1 when a question required rediscussion.

**Results:** Six rounds have been completed so far. Panelists agreed on the clinical workspace of the workflow (specialist outpatient service), the stage of application (prodromal and mild dementia), and the patient age window (biomarker use strongly encouraged below 70 years and of limited usefulness over age 85).

The workflow is patient-centred and features three levels of assessment (W): W1 defines eleven clinical profiles based on the integrated results of neuropsychology, MRI atrophy patterns, and blood tests; W2 describes the first-line biomarkers according to W1's clinical suspicion; and W3 suggests the second-line biomarker when the results of first-line biomarkers are inconsistent with the diagnostic hypothesis, uninformative or inconclusive. More specifically, CSF biomarkers are first-line in the suspect of Alzheimer's disease (AD) and when inconsistent neuropsychological and MRI findings hinder a clear diagnostic hypothesis; dopamine SPECT/PET for those leading to suspect Lewy body spectrum. FDG-PET is first-line for the clinical profiles leading to suspect frontotemporal lobar degeneration and motor tauopathies and is followed by CSF biomarkers in the case of atypical metabolic patterns, when an underlying AD etiology is conceivable.

**Conclusions:** The workflow will promote consistency in diagnosing neurocognitive disorders across countries, and rational use of resources. The initiative has an impact in preparing clinicians to work in the upcoming clinical space where etiological disease-modifying drugs are expected to be available.

P060

## The Effects of Vibro-Tactile Biofeedback Training on Balance Control and Dizziness in Patients with Persistent Postural Perceptual Dizziness (PPPD)

H. M. Rust <sup>1</sup>, C. Candreia <sup>2</sup>, F. Honegger <sup>3</sup> and J. H. Allum <sup>3</sup>

<sup>1</sup> Department of Neurology, University Hospital Basel, Switzerland

<sup>2</sup> Luzerner Kantonsspital, HNO-Klinik, Switzerland

<sup>3</sup> Universitätsspital Basel, Klinik für Hals-, Nasen-, Ohrenheilkunde, Switzerland

**Aims:** Patients with PPPD frequently report being “off-balance”. Artificial systems can provide sensory augmentation of natural sensory signals using vibro-tactile feedback (VT-fb) of trunk sway. Training with VT-fb is known to improve balance control in patients with vestibular deficits. The question arises whether such artificial systems improve balance control in PPPD patients. Therefore, we assessed the effects of VT-fb of trunk sway on balance control during stance and gait tests, and on perceived dizziness in PPPD patients.

**Methods:** Balance control in the form of trunk sway during 14 stance and gait tests was scored using a Balance Control Index (BCI) in 12 patients with PPPD of primary (N = 5) and secondary (N = 7) origin. Trunk sway in the pitch and roll planes was measured with a SwayStar System™. The Dizziness Handicap Inventory (DHI) was used to assess dizziness. Exclusion criteria were central vestibular lesions and the inability to walk up and down a set of 2 stairs. Subjects first underwent a standard balance assessment from which VT-fb thresholds were calculated. A headband mounted VT-fb system, connected to the SwayStar™ system, was active in 1 of the 8 directions when the threshold for that

direction was exceeded. Subjects trained with the feedback system twice per week for 30 min over a total of 2 consecutive weeks. The BCI and DHI were reassessed each week and the thresholds reset after the first week.

**Results:** All patients showed improved balance control after 1 and 2 weeks VT-fb training (22%  $p = 0.034$ , and 26%  $p = 0.008$ , respectively), regardless of whether the balance control was pathological prior to training. After 2 weeks, BCI values were significant less ( $p = 0.0001$ ) than the upper 95% limit of normal, age matched, reference values. Lower DHI values were also achieved after VT-fb training ( $p = 0.05$ ). A subjective benefit in balance control was spontaneously reported by 9 patients.

**Conclusions:** These initial results show that providing VT-fb of trunk to PPPD subjects yields a significant improvement in balance control and DHI assessed dizziness. The effect was present after 1 week of VT-fb training with further improvement after 2 weeks. Additional studies with higher numbers of participants are needed in order to assess whether VT-fb can be recommended for the treatment of PPPD in general or if this intervention benefits a specific subgroup of PPPD patients with a distinct presentation of this functional vestibular disorder.

P061

### Effect of Siponimod on Disability Progression as Measured by the Ambulation Score of the Neurostatus-EDSS: Post hoc Analysis of the EXPAND Trial in SPMS

M. D'Souza <sup>1</sup>, G. Giovannoni <sup>2</sup>, P. Vermersch <sup>3</sup>, S. Arnould <sup>4</sup>, S. Ansari <sup>5</sup>, G. Karlsson <sup>6</sup>, D. Piani-Meier <sup>6</sup> and L. Kappos <sup>7</sup>

<sup>1</sup> Neurologic Clinic and Polyclinic, Department of Head, Spine and Neuromedicine, University Hospital of Basel, Basel, Switzerland

<sup>2</sup> Blizzard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

<sup>3</sup> University Lille, INSERM U1172, CHU Lille, FHU Precise, Lille, France

<sup>4</sup> Novartis Pharmaceutical Corporation, East Hanover, NJ, USA

<sup>5</sup> Novartis Pharmaceuticals Corporation, Cambridge, MA, USA

<sup>6</sup> Novartis Pharma AG, Basel, Switzerland

<sup>7</sup> Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), Departments of Head, Spine and Neuromedicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital and University of Basel, Basel, Switzerland

**Aims:** To perform a post hoc analysis of the EXPAND trial data to assess the effect of siponimod on the Ambulation Score (AS) of the Neurostatus-Expanded Disability Status Scale (Neurostatus-EDSS) in secondary progressive multiple sclerosis (SPMS).

**Background:** More than 50% of Multiple Sclerosis (MS) patients transition to SPMS within 15–20 years, and disability continues to gradually worsen. Most currently available treatments do not consistently show efficacy in slowing disability progression independent of relapses. In the Phase 3 EXPAND study, siponimod reduced the Neurostatus-EDSS-measured risk of 3/6-months confirmed disability progression versus placebo by 21%/26%, with more pronounced effects (31%/37%) in active SPMS (aSPMS).

**Methods:** This post-hoc analysis included the overall population (siponimod/placebo  $n = 1099/546$ ) and aSPMS/non-active (naSPMS) patients (siponimod,  $n = 516/557$ , placebo,  $n = 263/270$ ). Outcomes included change from baseline in Neurostatus-EDSS/AS, time-to-first worsening on AS (3/6-months confirmed worsening [3M/6MCW]) by  $\geq 1/\geq 2$ -points and categorical analysis (proportion of patients with 3M/6MCW or confirmed improvement [CI] by  $\geq 1$ -point during the core study [median (range): 21 (0.2–37.0)M]).

**Results:** In the OP, the Neurostatus-EDSS, and more prominently, AS change from baseline, favored siponimod versus placebo at all visits (M6–M30); most pronounced at M18 (EDSS: 0.13 versus 0.23;  $p = 0.003$ , AS: 0.50 versus 0.81;  $p = 0.001$ ). Siponimod significantly reduced the risk of 3MCW ( $\geq 1$ -point, HR = 0.78,  $p = 0.0046$ ,  $\geq 2$ -point, 0.71,  $p = 0.0007$ ) and 6MCW in AS ( $\geq 1$  point, 0.74,  $p = 0.0023$ ). At M24, fewer patients

worsened/more improved on siponimod versus placebo (Neurostatus-EDSS: 6MCW, 26.9% versus 35.7%; 6MCI, 11.1% versus 8.5%,  $p = 0.03$ , AS: 6MCW, 33.4% versus 45.2%; 6MCI, 14.9% versus 10.6%,  $p = 0.005$ ). In aSPMS pronounced effects were observed in 3MCW ( $\geq 1$ -point, HR = 0.68,  $p = 0.002$ ,  $\geq 2$ -point, 0.60,  $p = 0.0005$ ); 6MCW ( $\geq 1$ -point, HR = 0.63,  $p = 0.0007$ ), with fewer patients worsening/more improving on siponimod and a trend for fewer patients worsening in naSPMS.

**Conclusions:** These findings corroborate siponimod's efficacy on disability progression in SPMS. More pronounced effects on the Neurostatus-EDSS and AS were observed in aSPMS and when using more stringent endpoint definitions. The Neurostatus-eEDSS is a standardized method to reduce inconsistencies and background noise of the neurological assessment and to reliably detect progression.

P062

### The CLEMENS Model of the Memory Centers of Canton Vaud: An Asset for Precision Medicine and Research

O. Rouaud <sup>1</sup>, D. Damian <sup>1</sup>, O. Daher <sup>2</sup>, R. Dreher <sup>3</sup>, P. Guillemin <sup>4</sup>, M. Nasuti <sup>1</sup> and G. Allali <sup>1</sup>

<sup>1</sup> Leenaard Memory Centre—CHUV, Switzerland

<sup>2</sup> Centre Mémoire et Gériatrie/Réseau Santé Nord Broye, Switzerland

<sup>3</sup> Centre Senior de La Côte/Réseau Santé La Côte, Switzerland

<sup>4</sup> Centre Mémoire/Réseau Santé Haut-Léman, Switzerland

**Introduction:** The canton of Vaud has established a network of three regional memory centers (CMr) coordinated by the Leenaards Memory Centre (CLM). Their missions is to diagnose neurocognitive disorders, to coordinate care with professionals and to contribute to research. This network began operating in 2014. All the centers make use of a computerized information system (CLEMENS), initially deployed at the CLM and, since 2019, at the 3 CMrs, for the collection of a standardized medical record. The system makes use of a diagnostic coding method adopted from the French National Alzheimer Database (BNA).

**Objectives:** To present the clinical activity of our network, the evolution of the diagnosis between 2019 and 2021 and the responses to our missions.

**Results:** 2246 patients (mean age: 72.2, 51.3% female) were examined in 2021 versus 1388 patients in 2014. In 2021, the mean MOCA score at the first consultation was 20.97 (20.24 in 2019); the proportion of patients under 65 yo was 28% (25.3% in 2019), 24.8% of patients were diagnosed with Alzheimer's disease or a related disease (ADRD) (25.3% in 2019) and 386 patients were diagnosed with AD (341 in 2019), 223 of whom (57.8%) were at the early stage. Amyloid positive status has been determined in 23% of patients. Between 2019 and 2021, 70 "complex" cases were referred by the CMr to the CLM for further investigations and 12 of those patients were included within existing research protocol(s).

**Discussion:** The increase of activity is explained by a public health need and the recognition of our expertise by GPs. The high MOCA value at the first consultation shows the effect of training in favor of early referral. A quarter of the patients are under 65 yo, which explains a high proportion of non-degenerative etiologies. Most of patients diagnosed with an underlying degenerative cause have an early-stage of AD. In 2021, the use of biological criteria made it possible to indicate an A+ status in almost one in four early-stage AD patients, which contribute to precision medicine for care and to the quality of data provided for research.

**Conclusions:** Our network is recognized for its expertise in the diagnosis and care of ADRD. Its organization allows patients, where the clinical needs justify it, to have access to biomarker and therapeutic innovation. In the near future, the CLEMENS model aims to expand throughout memory clinics across French-speaking Switzerland.

P063

## Object-Centered Sensorimotor Bias of Torque Control in the Chronic Stage Following Stroke

T. Schneider <sup>1</sup> and J. Hermsdörfer <sup>2</sup>

<sup>1</sup> Kantonsspital St. Gallen, Department of Neurology, Switzerland

<sup>2</sup> Technical University of Munich, Germany

When lifting objects whose center of mass (CoM) are not centered below the handle one must compensate for arising external torques already at lift-off to avoid object tilt. Previous studies showed that finger force scaling during object lifting may be impaired at both hands following stroke. However, torque control in object manipulation has not yet been studied in patients with stroke.

In this study, thirteen patients with chronic stage left hemispheric stroke (SL), nine patients with right hemispheric stroke (SR) and hand-matched controls had to grasp and lift an object with the fingertips of their ipsilesional hand at a handle while preventing object tilt. Object CoM and therewith the external torque was varied by either relocating a covert weight or the handle. The compensatory torque at lift-off ( $T_{com}$ ) is the sum of the torque resulting from 1) grip force being produced at different vertical finger positions ( $\Delta CoP \times GF$ ) and 2) different vertical load forces on both sides of the handle ( $\Delta Fy \times w/2$ ). When having to rely on sensorimotor memories,  $\Delta CoP \times GF$  was elevated when the object CoM was on the ipsilesional-, but decreased when CoM was on the contralesional side in SL, whereas  $\Delta Fy \times w/2$  was biased in the opposite direction, resulting in normal  $T_{com}$ . SR patients applied a smaller  $\Delta CoP \times GF$  when the CoM was on the contralesional side. Torques were not altered when geometric cues were available. The sensorimotor spatial bias of  $\Delta CoP \times GF$  was more pronounced and translated to a bias of overall  $T_{com}$  in SL patients with signs of apraxia ( $n = 3$ ).

Our findings provide evidence for an object-centered spatial bias of manual sensorimotor torque control with the ipsilesional hand following stroke. While both intact finger force-to-position coordination and visuomotor control may compensate for the spatial sensorimotor bias in most stroke patients, it may result in a hampered manual torque control in patients with apraxia.

P064

## Analysis of Plasma-Derived Extracellular Vesicles in a Mouse Model of Multiple Sclerosis

V. Lim Falk <sup>1</sup>, S. Joly <sup>2</sup>, A. Asadauskas <sup>1</sup>, I. Meli <sup>1</sup>, S. Spiegel <sup>1</sup>, A. Chan <sup>1</sup> and V. Pernet <sup>1</sup>

<sup>1</sup> Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

<sup>2</sup> Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

**Background and aim:** Extracellular vesicles (EVs) are cell-derived particles produced in physiological and pathological conditions (1). EVs have emerged as potent intercellular mediators and potential biomarkers in various diseases. In multiple sclerosis (MS) and in the mouse model of experimental autoimmune encephalomyelitis (EAE), an increased concentration of EVs in plasma and CSF has been observed (2–4). Studies also suggest an active role of EV cargoes in the inflammatory response of MS (5–7). However, it is not clear if EV-derived molecules can be used as specific biomarkers of disease activity in MS. Therefore, the aim is to examine the composition of plasma-derived EVs (pEVs) in EAE mice.

**Methods:** Adult C57BL/6J female mice were injected with myelin oligodendrocyte glycoprotein peptide (MOG35-55) to induce EAE together with Complete Freund's Adjuvant (CFA) and pertussis toxin (PTX) ( $n = 10$ ). Control groups were injected with

CFA/PTX (n = 10) or PBS (n = 10). Motor deficits and body weight were assessed daily. Mice were sacrificed in acute EAE, i.e., 15 days post-injection. Spinal cord demyelination was analyzed with luxol fast blue staining on paraffin sections. The isolation of pEVs was carried out with SmartSEC™ Single Kits. The concentration and size of pEVs were determined with the NanoSight nanoparticle tracking analysis system (NS300). EV-specific markers were detected by western blotting (WB).

**Results:** The size of pEVs was within the range of exosomes (EAE:  $106.4 \pm 6.2$  nm, CFA:  $93.3 \pm 2.8$  nm, PBS:  $119.5 \pm 11.1$  nm, mean  $\pm$  S.E.M.). The concentration of pEVs was similar to those reported in previous studies (EAE:  $5.0 \times 10^{10} \pm 2.40 \times 10^{10}$ , CFA:  $1.66 \times 10^{10} \pm 4.88 \times 10^9$ , PBS:  $1.69 \times 10^{10} \pm 4.63 \times 10^9$  particles/mL). Detection of the specific EV markers Alix, CD81, flotillin and CD9, and the absence of albumin, suggest a high purity of EV preparations. However, the concentration and size of pEVs did not significantly differ between EAE and control mice. Interestingly, preliminary WB results suggest that the neuronal growth inhibitor Nogo-A may be more abundant in the pEVs of EAE than in control mice.

**Conclusions:** Our results suggest that EAE does not significantly affect the concentration and size of pEVs. However, EAE may induce the secretion of brain-derived pEVs, as suggested by the upregulation of the CNS protein Nogo-A. Refined analyses are required to determine if the number of CNS cell-specific pEVs is higher in EAE than in control mice.

P065

### Impact of Post-COVID-19 Syndrome on Work Ability and Quality of Life: A Swiss Survey Study

L. F. Diem, A. Schwarzwald, C. Friedli, H. Hammer, L. Fregolente, J. Warncke, L. Weber, N. Kamber, A. Chan, C. Bassetti, A. Salmen and R. Hoepner

Inselspital, Bern University Hospital, University of Bern, Switzerland

**Introduction:** Post-COVID-19 syndrome affects approximately 10–25% of people after a COVID-19 infection, irrespective of initial COVID-19 severity. The aim of this study is to assess the impact of Post-COVID-19 syndrome on work ability and quality of life using an online survey.

**Methods:** The online survey of people with suspected and confirmed COVID-19 and Post-COVID-19 syndrome was distributed via Swiss COVID-19 support groups, social media and our Post-COVID-19 consultation. The analysis comprised 8 different domains with 120 questions in total. Data were collected from October 15, 2021 to May 14, 2022. In total, 543 people responded to our questionnaire and were included in the analyses (Mann-Whitney U Test, and Chi-Square-Test).

**Results:** The three most prevalent Post-COVID-19 symptoms in our survey cohort were fatigue (379/543, 69.8%), pain including headache (279/543, 51.4%) and sleep-wake disturbances (mainly insomnia and excessive daytime sleepiness, 202/543, 72.2%). Regarding fatigue severity, mean Fatigue Severity Scale (FSS) was 5.7 (95%CI 5.5–5.8, range 0.7–7, n = 378). Post-COVID-19 syndrome had an impact on work ability. About half of the respondents (184/384, 47.9%) reported an inability to work lasting on average 33.2 weeks (95%CI 30.1–36.3, range 1–105, n = 175). Quality of life measured by WHO-5 Well-being Index was overall low in respondents with Post-COVID-19 syndrome (mean, 95%CI 6.5 (6.0–7.0), range 0–25, n = 478).

**Conclusions:** Fatigue, pain and sleep-wake disturbances were the main symptoms of Post-COVID-19 syndrome in our survey and had an impact on quality of life and ability to work in a considerable proportion of patients. Post-COVID-19 syndrome remains a significant challenge. Further studies to characterise this syndrome and to explore therapeutic options are therefore urgently needed.



P066

### Clinical Course and Recurrence in Transient Global Amnesia: A Study from the TEMPiS Telestroke Network

S. Taheri <sup>1</sup>, R. Backhaus <sup>2</sup>, A. Zietz <sup>3</sup>, B. Abel <sup>4</sup>, F. Barinka <sup>1</sup>, F. Schlachetzki <sup>5</sup> and N. Peters <sup>1</sup>

<sup>1</sup> Stroke Center, Klinik Hirslanden, Zurich, Switzerland

<sup>2</sup> Swiss Clinical Neuroscience Institute, Zurich, Switzerland

<sup>3</sup> Department of Neurology and Stroke Center, University Hospital Basel, Switzerland

<sup>4</sup> Klinik Hirslanden Zürich, Switzerland

<sup>5</sup> Department of Neurology, Center for Vascular Neurology and Intensive Care, TEMPiS telestroke center, medbo Bezirksklinikum Regensburg, University of Regensburg, Germany

**Background:** Transient global amnesia (TGA) is characterized by a sudden loss of anterograde and short-term memory lasting up to 24 h. While the clinical hallmarks of TGA are well defined, the pathophysiologic causes are yet to be understood. Specifically risk factors of recurrences are yet to be determined.

**Methods:** Retrospective study of TGA cases diagnosed and treated within the (TEMPiS)-telestroke network, Germany. Demographic and clinical data were assessed and characteristics of TGA-episodes, such as seasonal occurrence, trigger factors, duration and concomitant symptoms were investigated. Follow-up regarding potential recurrence of TGA was assessed using a standardized questionnaire.

**Results:** Overall, 109 patients were included (mean age 64 +/- 8 years), 59.6% female). The most prevalent vascular risk factor was arterial hypertension (60.9%). Other concomitant conditions included migraine (11.9%), hypothyroidism (22.9%) and atrial fibrillation (4.6%).

The most frequent concomitant clinical feature that accompanied the TGA episode upon admission was elevated blood pressure (48.6%). A typical DWI-positive MRI lesion in the hippocampus was seen in 39.7% of patients with available MRI-data. Nineteen patients did experience one or more recurrent TGA episodes. Mean follow-up period was 40 months (median = 32.5).

Subjects with TGA-recurrence were older than those without recurrence (68.8. years vs. 63.3 years;  $p = 0.046$ ).

The two groups differed with respect to concomitant conditions: migraine and hypothyroidism were only observed in subjects with single TGA without recurrence (migraine: 14.4% without recurrence vs. none in the group with TGA recurrence;  $p = 0.02$  and hypothyroidism 27.8% without recurrence vs. none in the recurrence group,  $p = 0.009$ ). In contrast, atrial fibrillation was more prevalent in subjects with TGA recurrence (21.1.% vs. 1.1% in the TGA patients without recurrence,  $p < 0.001$ ).

**Conclusions:** Arterial hypertension is prevalent in TGA patients and elevated blood pressure was the most frequent concomitant condition. In our cohort, recurrence of TGA occurred in approximately one fifth of patients and patients were older than those without recurrence of TGA. Single and recurrent TGA were associated with different concomitant medical conditions, including migraine, hypothyreosis and atrial fibrillation. The underlying mechanisms of these findings remain undetermined and should be validated in future studies.

P067

### Case report: The Odyssey to the Right Diagnosis. Surprising Glioblastoma Mimicss

P. Dorin, W. Jochum, A. Lauber, T. Hundsberger

Kantonsspital St. Gallen, Switzerland

**Case:** A 57-year-old female presented at the emergency room with acute onset aphasia but unremarkable cCT (incl. angiography and perfusion). Suspecting an ischemic stroke, she received thrombolysis with quick recovery of aphasia. Afterwards, myoclonic jerks of the face and right arm occurred leading to anticonvulsant therapy. Follow-up cMRI surprisingly demonstrated swollen T2w-hyperintense and Gd-enhancing left limbic, temporal and frontal lobes. Suspected herpes-simplex-encephalitis was treated with aciclovir despite unremarkable CSF results (no pleocytosis, no BBB disruption, negative HSV-PCR) on day 2 and follow-up (day 5).

Due to persisting cognitive deficits, autoimmune limbic encephalitis was suspected, and intravenous immunoglobulin therapy was added. Three weeks later, she experienced new neurological symptoms (weakness, blurred vision, vomiting, headache). Follow-up brain MRI demonstrated a massive increase of multifocal Gd-enhancing lesions. Partial resection revealed the diagnosis of an IDH-wildtype glioblastoma (GB). Next generation oncogene panel testing demonstrated a GOPC-ROS1 fusion which is rarely found in GB. Due to the gliomatosis-like infiltration of both hemispheres, radiotherapy was deemed to be too toxic. Instead, she received two cycles of lomustine in absence of a MGMT-promotor methylation. Two months later cMRI showed a symptomatic second multilocular progression. 2nd-line therapy with a ROS-inhibitor was rejected, whereupon she died five weeks later.

Our case is in several aspects peculiar:

- It demonstrates that rare GB-mimics (i.e., HSV- and autoimmune limbic encephalitis) can only be ruled out in a fast manner by brain biopsy. Watchful waiting may neglect fast progression of GB leading to the inability to provide optimal treatment (i.e., radiotherapy).
- Thrombolysis is strictly contraindicated in primary brain tumors, but was unharmed in our case most probably to the early tumor stage without relevant neoangiogenesis.
- Rare genetic abnormalities like ROS1-fusions which are reported mostly in childhood glioblastoma may be present and serve as a therapeutic target also in adult GB.

P068

## Multiple Sclerosis-Related Fatigue and Eating Habits—A Prospective Observational Study

G. Thévoz <sup>1</sup>, J. Rebeaud <sup>1</sup>, A. Gauthier-Jaques <sup>1</sup>, P. Dubois-Ferriere <sup>1</sup>, T. Collet <sup>2</sup> and C. Pot <sup>1</sup>

<sup>1</sup> Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Switzerland

<sup>2</sup> Geneva University Hospitals (HUG) and University of Geneva (Unige), Switzerland

**Aim:** Multiple sclerosis (MS) is the most frequent non-traumatic neurological disease in young adults. Fatigue, a common and disabling MS symptom that occurs at all stages of MS disease remains difficult to treat and refractory to rest. While the role of nutrition in MS is debated, promising results in reducing fatigue have been suggested with diet management. However, there are still no solid evidences on how eating patterns act on MS. We here aimed to assess the relationship between fatigue in MS and eating duration and sleep quality. We hypothesized that a shorter eating duration could be beneficial to fight fatigue.

**Methods:** In a prospective observational study of 53 MS patients, eating duration was evaluated based on timestamped food and drink intake recorded with a smartphone application. Fatigue was assessed with EMIF-SEP questionnaire ranging from 0 (no fatigue) to 120 (maximum fatigue) and sleep with the Pittsburgh Sleep Quality Index (PSQI) ranging from 0 (excellent sleep quality) to 21 (very poor sleep). We performed Mann-Whitney U tests to evaluate if eating and sleep duration could influence MS-related fatigue.

**Results:** Among the 53 participants, the median age was 34 years old, 42 (79.25%) were women and, had a median disease duration of 22 months. The median expanded disability status scale (EDSS) was 1.5 and the median Body Mass Index 24.27 kg/m<sup>2</sup>. 45 participants (84.91%) were treated by disease-modifying therapies. Patients with a shorter eating duration reported more fatigue (EMIF-SEP median: 35.93, interquartile range [IQR]: 21.44–49.97, eating duration median: 14 h 10, IQR: 12 h 43–14 h 46) but with borderline significance ( $p = 0.055$ ). Shorter eating duration was associated with a longer sleep duration ( $p = 0.04$ ), and poor sleep quality was associated with more fatigue ( $p = 0.005$ ) while no correlation was observed between fatigue and sleep quantity ( $p = 0.11$ ).

**Conclusions:** In our cohort of MS patients with a low EDSS score, we observed an unexpected borderline association between a shorter eating duration and a higher fatigue score. A shorter eating duration was associated with a longer sleep duration and fatigue with a poor sleep quality. Several studies explored the influence of sleep on diet but there are few studies on the influence of eating habits on sleep quantity or eating duration. Thus the interconnection between eating and sleep duration remains to be evaluated and could lead to new approaches to fight fatigue in MS.

P069

### Histological Examination of Synaptotagmin 2 Changes in a Mouse Model of Multiple Sclerosis

A. Asadauskas <sup>1</sup>, S. Joly <sup>2</sup>, I. Meli <sup>1</sup>, J. B. Mdzomba <sup>1</sup>, A. Chan <sup>1</sup> and V. Pernet <sup>1</sup>

<sup>1</sup> Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Switzerland

<sup>2</sup> Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

**Background and aims:** Independently of axonal damage and demyelination, synaptic loss is thought to contribute to motor deficits in multiple sclerosis and in its animal model, experimental autoimmune encephalomyelitis (EAE). Resulting synaptopathy has been well characterized in the brain but much less in the spinal cord. In the spinal cord, synaptotagmin 2 (Syt 2) is a synaptic vesicle protein involved in fast Ca<sup>2+</sup>-dependent neurotransmitter release. The aim of the present study was thus to study Syt 2 variations in acute and chronic mouse EAE.

**Methods:** B cell-dependent EAE was induced in 8-week-old C57BL/6J male mice by injecting modified (S42P) myelin oligodendrocyte glycoprotein 1–125 (bMOG), Complete Freund's Adjuvant (CFA), and pertussis toxin (PTX). Motor symptoms/EAE clinical scores and body weight changes were daily followed. Mice were sacrificed in acute EAE, i.e., on day 14 ( $n = 10$ ), or in chronic EAE ( $n = 5$ ), on day 32 post-bMOG injection. Control mice received CFA/PTX ( $n = 5$ ). Demyelination was analyzed in spinal cord by staining paraffin sections with luxol fast blue. Adjacent histological sections were stained for Syt 2 by immunofluorescence.

**Results:** In acute EAE, the percentage of demyelination was significantly more severe in the lumbar ( $18.24 \pm 3.15\%$ , mean  $\pm$  S.E.M.) than in the cervical ( $10.79 \pm 2.18\%$ ) and thoracic ( $10.33 \pm 2.31\%$ ) spinal cord (ANOVA,  $p < 0.01$ ). The extent of demyelination in the cervical and lumbar spinal cord correlated with the motor symptoms at 14 days. In chronic EAE, demyelination was more pronounced in the lumbar ( $13.29 \pm 1.15\%$ , mean  $\pm$  S.E.M.) than in the thoracic ( $6.80 \pm 1.08\%$ ; ANOVA,  $p < 0.001$ ) but not in the cervical ( $11.43 \pm 2.02\%$ ) spinal cord. On day 32, motor symptoms were only detectable in 2 out of 5 mice, suggesting remission. During the acute phase, the immunofluorescent signal of Syt 2 was increased by ~72% in the lumbar spinal cord of EAE mice compared with CFA-treated mice (unpaired  $t$ -test,  $p < 0.05$ ). In the chronic phase, the signal of Syt 2 was increased by ~73% in the lumbar spinal cord (unpaired  $t$ -test,  $p < 0.05$ ). At the same time point, Syt 2 was increased by ~96% in the cervical spinal cord of EAE mice (unpaired  $t$ -test,  $p < 0.05$ ).

**Conclusions:** Syt 2 is upregulated in the spinal cord of EAE mice, especially in the lumbar region where EAE induces severe myelin loss. Further experiments are required to clarify the functional role of Syt 2 in EAE pathogenesis.

P070

### Progressive Ataxia and Palatal Tremor Due to a Novel Heterozygous GRIN2A Mutation

E. Ardila Jurado <sup>1</sup>, G. Kägi <sup>1</sup> and F. Brugger <sup>2</sup>

<sup>1</sup> Kantonsspital St. Gallen, Switzerland

<sup>2</sup> Kantonsspital St. Gallen, Switzerland

**Objective:** To describe the case of a patient with adult-onset progressive ataxia and palatal tremor (PAPT) in association with a novel heterozygous mutation of the GRIN2A gene.

**Background:** Progressive ataxia and palatal tremor (PAPT) is a clinical syndrome that may be caused by various acquired and inherited aetiologies. Lesions within the Guillain-Mollaret triangle of different aetiologies are known to account for the acquired causes, whereas mutations of the GFAP (Alexander's disease), POLG or SPG7 genes are among the most frequently reported genetic forms.

**Methods:** Case report.

**Results:** We present the case of a 56-year-old woman who presented with a palatal tremor and slowly progressive gait difficulties. The hyperkinetic movements were first observed by an ENT specialist who investigated her for a chronic pain of her right face. Furthermore, she complained about double vision for about 3 years. There was no family history of neurological diseases. On clinical examination, there was a palatal tremor with oscillatory movements at a frequency of approximately 2 Hz. The rhythmic movements also involved the hypopharynx and both vocal cords. There was also a rotational nystagmus of similar frequency. Furthermore she showed some mild dysarthria, mild cerebellar oculomotor features, dysdiadochokinesia and pyramidal signs. On walking she suffered from mild gait ataxia. Her MRI showed hyperintensities of both inferior olives along with an olivary hypertrophy, but without evidence of a lesion such as a tumour. Her CSF including Whipple-PCR and antineuronal antibodies was normal. Her EEG did not show any abnormalities. A whole exome sequencing revealed a heterozygous pathogenic deletion of exon 6 of the GRIN2A gene (c.1422\_1425delTTAC/p.(Tyr475Thrfs\*5)).

**Conclusions:** GRIN2A mutations should be considered as a potential cause for genetic forms of adult-onset PAPT. The gene was previously described in relation to the epilepsy-aphasia spectrum. Our patient shows a different phenotype as the originally described syndrome with no epilepsy and a normal EEG. However, ataxia and hyperkinetic movement disorders including orolingual movement abnormalities were mentioned as infrequent symptoms in a large series of cases with GRIN2A mutations (Strehlow et al., 2018). We propose that our case broadens the clinical spectrum of disorders due to mutations in this gene. Further studies are needed to confirm GRIN2A mutations as a cause for a predominant PAPT phenotype.

P071

### Post-Stroke Dysphagia: A Systematic Review of RCT on Interventional Treatments for Dysphagia Following Subacute Stroke

P. Balcerak, S. Corbière, R. Zubal, G. Kägi

Kantonsspital St. Gallen, Switzerland

**Aims:** Dysphagia is a frequently encountered symptom of stroke survivors. It is associated with a worse clinical outcome, dependency and quality of life. The detailed underlying mechanisms are not very well understood. Therapeutical guidelines on this topic are missing, but concepts are needed. Various interventional studies dealing with post-stroke dysphagia have been published, using different therapeutical concepts. This systematic review wants to collect them and give an overview of the existing evidence.

**Methods:** Four databases (PubMed, Embase, Cochrane, CINAHL) were searched for relevant studies in English on post-stroke dysphagia. Randomized interventional trials which contain an inactive control and deal with post-stroke dysphagia in the (sub-)acute phase (within 3 months of stroke onset) were included. The relevant data was extracted, and the methodological quality was assessed.

**Results:** After screening of 2863 trials, finally 41 trials have been included. 7 different therapeutic concepts have been evaluated (Acupuncture, behavioural/physical therapy, drug therapy, neuromuscular electrical stimulation, pharyngeal electrical stimulation, transcranial direct current stimulation and repetitive transcranial magnetic stimulation). Various studies of all modalities have shown effect on post-stroke dysphagia to some extent. But in most studies there was a relevant concern on the bias.

**Conclusions:** The amount and quality of studies are not enough to suggest certain therapies. Some therapeutical concepts (intensive physical therapy, transcranial magnetic stimulation, drug therapy) seem to be good potential therapeutic options, but the methodological quality is insufficient. In this review some promising therapeutical concepts have been presented, but further research is needed.

P072

### **A Rare Cause of Triggered Episodic Vestibular Syndrome and Transient Loss of Consciousness—Retrostyloidal Vagal Schwannoma**

**M. Spiegelberg<sup>1</sup>, E. Ermis<sup>2</sup>, A. Raabe<sup>3</sup> and A. Tarnutzer<sup>1</sup>**

<sup>1</sup> Kantonsspital Baden AG, Switzerland

<sup>2</sup> Inselspital und Universität Bern, Switzerland

<sup>3</sup> Inselspital, Switzerland

**Aim:** Various conditions may trigger episodic vertigo or dizziness, with positional changes and specific locations being most frequently identified conditions. Here we describe a rare cause of triggered episodic dizziness that sometimes was followed by transient loss of consciousness (TLOC) in a patient diagnosed with a retrostyloidal vagal schwannoma.

**Case description:** A 27-yo women presented with nausea, right-sided dysphagia and odynophagia and recurrent TLOC (with prodromal cold sweats, pallor, palpitations) when swallowing solid food, resulting in a weight-loss of 10 kg over 12 months. Furthermore, she noticed an exacerbation of her chronically, intermittent right-sided tinnitus. These symptoms occurred independently of her body position and she could not prevent the vagovasal reflex syncope with typical “prevention maneuvers”. An extensive cardiologic diagnostic work-up was normal. The neuro-otologic assessment including fiberoptic endoscopic evaluation of swallowing demonstrated a decreased sensitivity of the right lateral pharyngeal wall, a slight bulging of the right lateral pharyngeal wall and a pathological pharyngeal squeeze maneuver without any further functional deficits. Quantitative vestibular testing revealed intact peripheral-vestibular function. On brain MRI a 16× 15× 12 mm lesion in the right retrostyloidal space suspicious of a vagal schwannoma was detected. With no expression of SSTR2 in a 68-Ga-DOTA-peptide PET/CT, a paraganglioma or glomus vagal tumor was considered unlikely. Treatment options were discussed at the interdisciplinary schwannoma board and a single radiosurgical procedure (stereotactic radiosurgery, CyberKnife®, 1× 13Gy) accompanied

by oral steroids over 16 days was proposed. This treatment was tolerated well by the patient. While at first follow-up 6 weeks after treatment the patient reported a slight reduction of (pre-)syncope, she also noticed emergence of diffuse dizziness and fear of syncope.

**Conclusions:** With a broad differential diagnosis of triggered episodic vestibular syndromes, structured history taking and identifying specific triggers is essential. In case of episodes being triggered by swallowing solid foods and accompanied by (pre-)syncope, search for a vagal schwannoma is essential, as symptoms may be disabling and targeted treatment is available. Due to the benign nature, a late response after radiosurgical procedure (>6 months) is anticipated, thus the outcome will be re-assessed on further follow-up.

P073

### **Persistent Improvement of Quality of Life and Pain Severity up to One Year Following Virtual Walking Therapy in a Patient with Neuropathic Pain after Spinal Cord Injury: A Case Report**

**K. Ottiger-Böttger**<sup>1</sup>, **R. Abächerli**<sup>2</sup>, **M. Ernst**<sup>1</sup>, **A. Ljutow**<sup>1</sup> and **G. Landmann**<sup>1</sup>

<sup>1</sup> Swiss Paraplegic Centre, Switzerland

<sup>2</sup> Lucerne University of Applied Sciences and Arts–Engineering and Architecture, Switzerland

**Aims:** Virtual walking (VW) is a novel therapy based on Graded Motor Imagery (GMI) using a third-person perspective, semi-immersive illusory walking training program to treat chronic neuropathic pain after spinal cord injury (SCIP). The aim was to evaluate the efficacy of VW and long term effects up to one year.

**Methods:** A 31-year old man with complete sensori-motor paraplegia L1, AIS A was monitored. VW was applied over six weeks: two weeks with five, two weeks with three and finally two weeks with two therapy sessions per week. Demographic and clinical data were collected prior therapy. Psycho-social questionnaires were applied prior, three and twelve months after VW. Pain diary was kept up to three months after VW. Pain was assessed using an 11-point numeric rating scale. Pain chronification was assessed by Chronic Pain Grade questionnaire (CPGQ). Pain interference with daily activities, mood and sleep was obtained. Psychological status was assessed using the Depression, Anxiety and Stress Scale (DASS), the Pain Catastrophizing Scale (PCS) and the “Marburger Fragebogen zum habituellen Wohlbefinden” (MFHW) to estimate habitual well-being. Health-related quality of life was evaluated by WHO-QoL-3 questionnaire.

**Results:** Three months after VW there was an improvement in pain intensity, a reduced pain area, an improvement of CPGQ severity grades, pain interference for sleep and mood and pain catastrophizing. DASS depicted a decrease of depression and stress symptoms and there was an amelioration of habitual well-being illustrated by MFHW. QoL showed an amelioration in the life and body domain. After 12 months, the scores from most questionnaires returned almost to the level of pre-treatment. However, habitual well-being and pain catastrophizing still indicated an amelioration. In addition, CPGQ continued with lower severity grade.

**Conclusions:** The results indicate that VW is an alternative treatment option which can lead to pain amelioration and long-lasting improvements in quality of life and pain severity in patients with neuropathic SCIP. However, more data from SCI patients is needed to evidence the effectiveness and therapeutic benefit of this novel therapy.

P074

**Rapidly Progressive Alzheimer's Disease in the Lausanne Memory Clinic Registry****P. Salvioni Chiabotti, M. Nasuti, G. Allali, O. Rouaud**

Centre Leenaards de la Memoire, Switzerland

Cognitive decline is the cardinal symptom of Alzheimer's disease (AD), the most common cause of dementia in elderly people worldwide. Even though many efforts were made to estimate its progression rate, the expected evolution is a daily clinical challenge and one of the main concerns for patients and relatives, highlighting the need for tailored approaches, anticipating care needs and decision-making.

Using the recent definition of rapidly progressive AD (rpAD; Schmidt C et al. Arch Neurol 2011;68:9) as a model for faster decline (loss of 3 or more points in the MMSE during a 6 month period), we aim at identifying factors that could distinguish these patients from other AD patients, in a Memory Clinic setting.

We retrospectively included AD patients included in the Lausanne Memory Clinic registry (CLEMENS), from its creation in 2013 to 2022. After stratifying them according to the rpAD definition (adapted to MoCA, using a well-established conversion table; Trzepacz et al. BMC Geriatrics. 2015;15:107) into two subgroups, we compared demographics, initial clinical presentation, MRI evidence of atrophy, co-occurrence of other disorders as well as  $\beta$ -42 amyloid, tau and P-tau values in CSF between rpAD and typically progressive AD.

From the 2319 patients collected on the registry, AD was the final diagnosis in 501 (21%). Only 221 had two consecutive cognitive evaluation and therefore 43 were rpAD (19.5% 1.8%) and 173 typically progressive AD (7.5%). No difference in age (mean 75.5 vs. 77.1 years), gender and education years was noted. While initial cognitive score and disease stage were non-discriminatory (mean MoCA score 21.3 vs. 20.1), rpAD patients had a tendency toward diffuse cognitive deficits at first neuropsychological assessment (28% vs. 17%), more frequent conversion from mild cognitive impairment to dementia throughout follow-up (33% vs. 20%). The presence of other disorders and their nature (whether neurological, psychiatric or systemic) was also non-discriminatory. No difference was observed neither in the global and hippocampal atrophy nor in CSF  $\beta$ -42 amyloid, tau or P-tau concentrations between groups, although morphological MRI data and CSF values were available for a limited number of patients.

In contrast to previous published data (Schmidt C et al. JAD. 2012;30:4, Lopez OL et al. Alzheimer's & Dementia. 2010;6:6, Snider BJ et al. Arch neurol. 2009;66:5), our retrospective monocentric registry study could.

P075

**Analyses of Genetic Haplotypes Related to Cognitive Decline in Parkinson's Disease (PD)****I. Cosentini <sup>1</sup>, A. Meyer <sup>2</sup>, M. Malaquini Stamato <sup>1</sup>, U. Gschwandtner <sup>3</sup> and P. Fuhr <sup>1</sup>**<sup>1</sup> Universitätsspital Basel, Switzerland<sup>2</sup> Universitätsspital Basel, Switzerland<sup>3</sup> Universitätsspital Basel, Switzerland

**Aims:** Parkinson's disease is not only characterized by motor disturbances, but also by a cognitive decline that occurs over time. Such cognitive decline is thought to be associated with certain genetic variations. APOE gene has been strongly correlated with Alzheimer disease and could therefore represent a risk factor in cognitive decline also in Parkinson's disease. We aim to find a correlation between the presence of specific haplotypes of APOE

and MAPT genes and the cognitive decline in Parkinson's disease patients and how the cognitive decline evolves over time.

**Methods:** We analyzed the Basel cohort, composed at baseline of 77 patients with PD (26 f, 51 m, age M 66 y (34–84 y), education M 15 y (9–20 y) and 30 health controls (13f, 17m, age M 66 y (56–75 y, education M 13.5 y (9–19 y)). The subjects have been followed up after 3 and 5 years. For cognitive screening, we used MMS and MoCa tests (total score and specific cognitive items). We correlated cognitive performance with the presence of E2, E3 and E4 haplotypes (APOE) and H1, H2 (MAPT) (collected with Neurochip X). Analyses were carried out comparing the performance of patients versus controls and of patients who were categorized as MCI (mild cognitive impaired) versus those categorized as cognitive normal at different time points.

**Results:** In the population, mainly composed of carriers of the homozygous form of APOE gene and the homozygous form of MAPT gene, we could only find a slight association between the presence of the haplotypes and the cognitive performance (MoCa Visuospatial PD vs. HC  $p < 0.005$ ). In the next step, we intend to combine APOE E4 carriers with MAPT H1 carriers.

**Conclusions:** Genetic analyses could give hints in detecting risk factors for cognitive decline in PD patients, but to find a stronger and possibly more reliable correlation more subjects would be needed to improve the power of risk factors and additionally, the subjects should be followed for a longer time.

P076

### Small Vessel Vasculitis with Predominant Central Nervous System Involvement Stabilizing with Anti-IL-6 Receptor Treatment—A Case Report

B. Birner<sup>1</sup>, S. Haumann<sup>1</sup>, T. R. Meinel<sup>1</sup>, A. Maurer<sup>1</sup>, C. Friedli<sup>1</sup>, H. Hammer<sup>1</sup>, L. Diem<sup>1</sup>, N. Kamber<sup>1</sup>, T. Maragkou<sup>2</sup>, B. Dislich<sup>2</sup>, D. Merkler<sup>3</sup>, B. Maurer<sup>4</sup>, A. Chan<sup>1</sup>, R. Hoepner<sup>1</sup> and A. Salmen<sup>1</sup>

<sup>1</sup> Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

<sup>2</sup> Department of Pathology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

<sup>3</sup> Department of Pathology, University Hospital Geneva, University of Geneva, Geneva, Switzerland

<sup>4</sup> Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

**Aims:** Small vessel vasculitides are a heterogeneous group of rare autoimmune diseases, comprising e.g., anti-neutrophil cytoplasmic antibody (ANCA-) associated or immune complex vasculitides. We describe the successful treatment of a patient with small vessel vasculitis with predominant central nervous system (CNS) involvement with tocilizumab.

**Methods:** Case report including clinical, serological, imaging and histology data.

**Results:** A 64-years old female patient presented with fever of unknown origin, elevated humoral inflammatory markers and weight loss of 20 kg within 5 months since symptom onset at hospital admission. Her family reported about gait instability and apathy. Clinically, she presented with severe psychomotor slowing, affective disturbances and a slight right-sided hemiparesis. Her medical history included curatively treated breast cancer and seronegative oligo-arthritis. Magnetic resonance imaging (MRI) of thorax and abdomen was performed. Whereas no large vessel vasculitis was found herein, 3 tesla cranial MRI revealed contrast-enhancement of perivascular spaces, wide-spread and focal white matter hyperintense lesions in the subcortical and deep white matter on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images, mainly suggestive of autoimmune glial fibrillary acidic protein astrocytopathy (GFAP) or small vessel vasculitis. Laboratory examination still showed signs of humoral inflammation. Cerebrospinal fluid (CSF) analysis demonstrated a slight pleocytosis, elevated protein and very high interleukin-6 (IL-6) levels. Brain biopsy was indicative of small vessel vasculitis. Treatment with systemic high-dose glucocorticoids (GC) and oral maintenance (1 mg/kg



bodyweight) led to an initial clinical and MRI response. Treatment with tocilizumab (400 mg every 4 weeks) was initiated due to ongoing severe disease and GC side effects. Further rapid MRI and clinical improvement was seen within 5 weeks. Tocilizumab is continued with GC tapering.

**Conclusions:** With negative GFAP antibodies (serum, CSF) and compatible brain biopsy results, small vessel vasculitis was diagnosed not fulfilling the main classification types. Add-on treatment with tocilizumab stabilized the patient. One supporting argument for the choice of tocilizumab was based on the very high level of IL-6 in CSF. Our case adds to single reports of IL-6 receptor blockade in vasculitis, being the first report in a patient with small vessel disease and predominant CNS affection.

P077

### Impact of Ofatumumab in Early RMS under Routine Medical Care: Phase 4 KOSMOS Study Design

N. F. Schäfer <sup>1</sup>, A. Meisterernst <sup>2</sup>, I. Meyer <sup>1</sup> and M. E. Arzt <sup>1</sup>

<sup>1</sup> Novartis Pharma Schweiz AG, Switzerland

<sup>2</sup> Clinipace AG, Switzerland

**Introduction:** Ofatumumab, an anti-CD20 antibody targeting B cells, received European (EMA and Swissmedic) marketing authorization in 2021 for the treatment of adult patients with active, relapsing forms of multiple sclerosis (RMS). However, prospective real-world data are still lacking. Here, we present the design of the KOSMOS study (Kesimpta [Ofatumumab] in Swiss Multiple sclerosis patients—an Observational Study; NCT05285904).

**Objectives:** To describe the effect of ofatumumab in an early patient population with RMS under routine medical care.

**Aims:** To collect real-world evidence about Ofatumumab's efficacy and safety profile, as well as adherence and patient-reported outcomes in patients treated with ofatumumab.

**Methods:** KOSMOS is a non-interventional, multi-centre study that enrolls RMS patients in Switzerland who initiated treatment with ofatumumab within 3 years of diagnosis of MS and as per Swiss label and local clinical practice. At inclusion into the study, patients must have received ofatumumab for at least 3 months, but not more than 12 months. Data are collected at 2 visits spanning an observation period of 12 months. The primary endpoint is "No Evidence of Disease Activity" (NEDA-3) at 12 months (no relapse, no new/enlarging lesions, no disability worsening), as compared to the "standard of care" treatment arm of a European phase 3b study, STHENOS. Secondary endpoints include NEDA-3 compared to the ofatumumab arm of STHENOS, adherence as measured by a disposal container equipped with sensors, as well as quality of life and treatment satisfaction. Optional exploratory endpoints include changes in the immune cell repertoire, serum biomarkers, and the ability to mount immunity to vaccinations.

**Results:** The KOSMOS study received approval by the lead ethics committee on 16 March 2022. As of submission of this abstract, 17 study sites have been contracted, of which 10 have been opened. 1 of 149 patients have been enrolled (first-patient-first-visit 12 May 2022), with the goal to complete recruitment by late 2023. Primary results are expected in 2025.

**Conclusions:** KOSMOS is designed to collect real-world evidence on ofatumumab and close the gap to phase 3 by direct comparison to a closely supervised clinical trial setting. As ofatumumab is self-administered by patients through an auto-injector pen at home, this study will provide valuable information on the effects of ofatumumab under routine medical care.

P078

### Subarachnoid Haemorrhage Due to a Spinal Aneurysm: A Case Report

B. Wagner <sup>1</sup>, D. Leupold <sup>1</sup>, O. Bozinov <sup>2</sup>, J. Weber <sup>3</sup> and J. Vehoff <sup>1</sup>

<sup>1</sup> Kantonsspital St. Gallen, Department of Neurology, Switzerland

<sup>2</sup> Kantonsspital St. Gallen, Department of Neurosurgery, Switzerland

<sup>3</sup> Kantonsspital St. Gallen, Department of Neuroradiology, Switzerland

**Introduction:** 85% of atraumatic subarachnoid haemorrhages (SAH) happen due to aneurysms (40% anterior communicating, 30% internal carotid, 20% middle cerebral and 10% basilar artery). Spinal aneurysms are extremely rare. We report a case of a patient who suffered from SAH due to a ruptured spinal aneurysm.

**Case Report:** A 68-year-old man reported a fronto-occipital thunderclap headache, followed by nausea and vomiting. Six days later, he noticed sudden onset left-sided weakness with spontaneous remission.

On admission, the neurologic exam was unremarkable. Non-contrast CT scan showed no signs of intracranial haemorrhage or ischemia. CT-angio showed vessels with calibre irregularities, a dissection of the left internal carotid artery and an aneurysm of the right anterior communicating artery of 4×3×3 mm in size. Lumbar puncture revealed a xanthochromic CSF with 4000 red blood cells per microliter, suggesting recent SAH. MR imaging detected infratentorial superficial siderosis. Duplex sonography revealed vasospasms. The patient was transferred to the neurosurgical department to perform clipping of the anterior communicating aneurysm, which was believed to have caused the SAH. During clipping of the aneurysm, surprisingly no signs of supratentorial SAH could be found. The aneurysm showed no signs of rupture; clipping was performed anyway without complications. With no bleeding source being found, a MRI long spine was performed, showing subdural haematoma and arachnoid post-haemorrhagic septa, extending from Th 2 to L1. A spinal angiography could detect a 2 millimetre sized, paramedullary aneurysm at Th 6.

Due to location and size, weighing pros and cons, a conservative treatment regimen was decided. A follow-up MR-A and another conventional angiography three months later showed no signs of the spinal aneurysm anymore and no increase in superficial siderosis.

**Discussion:** The combination of aneurysms, calibre irregularities and dissection of the left internal carotid artery suggests an underlying vasculopathy. No signs of systemic rheumatologic disease could be found.

Spinal aneurysms are a rare cause of SAH. Especially in infratentorial SAH and no other bleeding source, further work-up is warranted. There is limited evidence on therapeutic strategies for spinal aneurysms. A conservative approach with clinical and imaging follow-up might be reasonable.

P079

### Reduced Alpha Suppression & Altered EEG Signal Complexity in Parkinson's Disease (PD) – Signature of Cognitive Impairment?

S. Keller <sup>1</sup>, A. Meyer <sup>2</sup>, U. Gschwandtner <sup>3</sup> and P. Fuhr <sup>4</sup>

<sup>1</sup> Universitätsspital Basel, Switzerland

<sup>2</sup> Universität Basel Spital, Switzerland

<sup>3</sup> Universitätsspital Basel, Switzerland

<sup>4</sup> Universitätsspital Basel, Switzerland

**Aims:** In a cross-sectional setting both alpha suppression and complexity of alpha-band oscillations are evaluated as diagnostic biomarker for assessing MCI in early stages of PD.

In a healthy human brain alpha-band oscillatory activity (8–13 Hz) is present during eyes closed (EC) condition but is suppressed when eyes are open (EO). Alpha oscillations have an important role in attentional processes. In PD, cognitive decline may be accompanied by pathological levels of attention. Therefore, the state of mild cognitive impairment (MCI) in PD, which is a transitional state between normal cognition (PD-NC) and overt dementia (PD-D), is hypothesized to exhibit abnormal behaviour compared to healthy controls or PD-NC patients.

**Methods:** 24 healthy controls (HC, 9 females, medians: age 66.5 yrs., edu. 14 yrs.) and 31 PD-NC individuals (14 females, medians: age 69.0 yrs., edu. 14 yrs., UPDRS 15, LED 490.0, disease duration 32 mos.) were compared with 8 individuals diagnosed with PD-MCI matched for age, sex and education (3 females, medians: age 65.5 yrs., edu 16 yrs., UPDRS 15.5, LED 784.5, disease duration 50 mos.). High-density EEG recordings were obtained during eyes open (EO) and eyes closed (EC) condition. Signal complexity quantified based on Tsallis entropy (TE), as well as relative band power (rBP) were evaluated for the alpha band. The resulting signal complexity and band power values were then compared across groups where grouping was based on an individuals' diagnosis.

**Results:** Evaluation of rBP during EC and EO condition showed significant or close to significant intra-group differences for HC ( $p = 0.00001$ ) and PD-NC ( $p < 0.0501$ ) but not for PD-MCI ( $p > 0.5$ ). Alpha band signal complexity is increased in EO condition across all groups compared to EC. While the PD-MCI group exhibited a non-significant increase ( $p > 0.9$ ), HC and PD-NC showed significant differences (HC:  $p = 0.0001$  and PD-NC:  $p = 0.003$ ).

**Conclusions:** In conclusion, mild cognitive impairment in PD may manifest in the alpha band (8–13 Hz) through impaired ability to perform alpha suppression and through increasingly similar levels of signal complexity between EC and EO condition. The results apply to groups and may help to define study populations for clinical trials, but cannot be applied in their present form for individual treatment decisions or counseling.

P080

## Natural History of Meningiomas—A Serial Volumetric Analysis of 240 Tumors

P. Thomann<sup>1</sup>, L. Häni<sup>1</sup>, S. Vulcu<sup>1</sup>, A. Schütz<sup>1</sup>, M. Frosch<sup>2</sup>, C. M. Jesse<sup>1</sup>, M. El-Koussy<sup>3</sup>, N. Söll<sup>1</sup>, A. Hakim<sup>1</sup>, A. Raabe<sup>1</sup> and P. Schucht<sup>1</sup>

<sup>1</sup> Inselspital, Bern University Hospital, Bern, Switzerland

<sup>2</sup> Medical Center—University of Freiburg, Switzerland

<sup>3</sup> Spital Emmental, Switzerland

**Aims:** The management of asymptomatic intracranial meningiomas is controversial. Through the assessment of growth predictors, we aimed to create the basis for practicable clinical pathways for the management of these tumors.

**Methods:** We volumetrically analyzed meningiomas radiologically diagnosed at our institution between 2003 and 2015. For this purpose, we used exclusively thin-layered MR images (i.e.,  $\leq 2$  mm slice thickness). The primary endpoint was tumor growth defined as a 14.35% increase in tumor volume. We identified predictive clinical and radiological characteristics and used the significant variables from a multivariable regression model to construct a decision tree based on the exhaustive Chi-squared Automatic Interaction Detection (exhaustive CHAID) algorithm.

**Results:** Of 240 meningiomas, 159 (66.3%) demonstrated growth during a mean observation period of 46.9 months. On multivariable logistic regression analysis, older age (OR = 0.979 (0.958–1.000),  $p = 0.048$ ) and presence of calcification (OR = 0.442 (0.224–0.872),  $p = 0.019$ ) had a negative predictive value for tumor growth, while T2-signal iso-/hyperintensity (OR = 4.415 (2.056–9.479),  $p < 0.001$ ) had a positive predictive value. A decision tree model yielded three growth risk groups based on T2-signal intensity and

presence of calcifications with a proportion of growing tumors of 34.1% in the low risk group, 60.0% in the intermediate risk group and 80.2% in the high risk group. Median tumor volume doubling time (Td) was 185.7 months in the low risk, 100.1 months in the intermediate risk and 51.7 months in the high risk group ( $p < 0.001$ ). While 0% of meningiomas in the low and intermediate risk group had a Td of  $\leq 12$  months, 8.9% in the high risk group did so ( $p = 0.021$ ).

**Conclusions:** Most meningiomas demonstrated growth during follow-up. The presence or absence of calcifications and the signal intensity on T2-weighted imaging allow a practical and simple stratification of meningiomas into low, intermediate and high risk tumors. Small tumors in the low or intermediate risk categories can be monitored with longer follow-up intervals, whereas in the high risk category proactive management decisions can be justified.

P081

### Successful Weaning vs. Permanent Cerebrospinal Fluid Diversion after Aneurysmal Subarachnoid Hemorrhage—Post-Hoc Analysis of a Swiss Multicenter Study

A. El-Garci <sup>1</sup>, O. Zindel-Geisseler <sup>2</sup>, N. Dannecker <sup>2</sup>, Y. R. Rothacher <sup>2</sup>, L. Schlosser <sup>2</sup>, J. Velz <sup>3</sup>, M. Sebök <sup>3</sup>, N. Eggenberger <sup>3</sup>, A. May <sup>4</sup>, P. Bijlenga <sup>4</sup>, U. Guerra-Lopez <sup>4</sup>, R. Maduri <sup>5</sup>, V. Beaud <sup>6</sup>, D. Starnoni <sup>6</sup>, A. Chiappini <sup>7</sup>, S. Rossi <sup>7</sup>, T. Robert <sup>7</sup>, S. Bonasia <sup>8</sup>, J. Goldberg <sup>9</sup>, C. Fung <sup>9</sup>, D. Bervini <sup>9</sup>, N. Maldaner <sup>3</sup>, K. Gutbrod <sup>9</sup>, O. Bozinov <sup>8</sup>, M. C. Neidert <sup>8</sup>, P. Brugger <sup>3</sup>, E. Keller <sup>3</sup>, M. R. Germans <sup>3</sup>, L. R. Regli <sup>3</sup>, I. C. Hostettler <sup>8</sup> and M. N. Stienen <sup>8</sup>

<sup>1</sup> Cantonal Hospital St. Gallen, St. Gallen, Switzerland

<sup>2</sup> University Hospital Zurich, Zurich, Switzerland

<sup>3</sup> University Hospital Zurich, Zurich, Switzerland

<sup>4</sup> University Hospital Geneva, Geneva, Switzerland

<sup>5</sup> Swiss Medical Network, Clinique de Genolier, Genolier, Switzerland

<sup>6</sup> University Hospital Lausanne, Lausanne, Switzerland

<sup>7</sup> Cantonal Hospital Lugano, Lugano, Switzerland

<sup>8</sup> Cantonal Hospital St. Gallen, St. Gallen, Switzerland

<sup>9</sup> University Hospital Berne, Berne, Switzerland

**Aim:** Acute hydrocephalus is a frequent complication after aneurysmal subarachnoid hemorrhage (aSAH). Of all patients needing cerebrospinal fluid (CSF) diversion some cannot be weaned. Little is known about the comparative neurological, neuropsychological and health-related quality of life (hrQoL) outcomes in patients comparing successful and unsuccessful CSF weaning. We aimed assess outcomes of patients comparing successful and unsuccessful CSF weaning, defined as patients with permanent CSF diversion at 3 months post-aSAH.

**Methods:** We included prospectively recruited alert (Glasgow Coma Scale of 13–15) aSAH patients from six Swiss neurovascular centers (ClinicalTrials.gov Identifier NCT03032471), who underwent serial neurological (National Institute of Health Stroke Scale; NIHSS), neuropsychological (Montreal Cognitive Assessment; MoCA), disability (modified Rankin Scale) and hrQoL-examinations (Euro-Qol 5D) < 72 h, 14–28 days and three months post-aSAH.

**Results:** Of 126 included patients, 54 (42.9%) developed acute hydrocephalus needing CSF diversion, of whom 37 (68.5%) could be successfully weaned and 17 (31.5%) required permanent CSF diversion. Patients with unsuccessful weaning were older (64 vs. 51 years,  $p = 0.001$ ) and had a higher rate of intraventricular hemorrhage (52.9% vs. 24.3%,  $p = 0.04$ ). Patients who succeed in restoration of physiological CSF dynamics improve on average by 2 points on the MoCA between 48–72 h and 14–28 days, whereas those who fail weaning worsen by 4 points (adjusted coefficient 6.80, 1.57–12.04 95%CI,  $p = 0.01$ ). They show better neuropsychological recovery between 48–72 h and 3 months, compared to

patients who fail weaning (adjusted coefficient 7.60, 3.09–12.11 95%CI,  $p = 0.02$ ). Patients that receive permanent CSF diversion (VP-shunt) show significant neuropsychological improvement, thereafter, catching up the delay in neuropsychological rehabilitation between 14–28 days and 3 months post-aSAH. Neurological, disability and hrQoL-outcomes at 3 months were similar.

**Conclusions:** Our results show a temporary but clinically meaningful cognitive benefit in the first weeks after aSAH in successfully weaned patients. This difference resolves over time maybe due to the positive effects of permanent CSF diversion. Patients, who do not show progressive neuropsychological improvement after weaning should be considered for repeat CT imaging to rule out chronic (untreated) hydrocephalus.

P082

### Proteomic Analysis of Glioma Biopsies Shows Consistency with Glioma Grading

M. Amer Salem <sup>1</sup>, J. Boulay <sup>1</sup>, M. Ritz <sup>1</sup>, F. S. Halbeisen <sup>2</sup>, A. Schmidt <sup>3</sup>, K. Buczak <sup>3</sup>, G. Hutter <sup>4</sup> and S. Leu <sup>4</sup>

<sup>1</sup> Brain Tumor Immuno-Therapy and Biology Laboratory, Department of Biomedicine, University Hospital of Basel, University of Basel, Basel, Switzerland

<sup>2</sup> Basel Institute for Clinical Epidemiology and Biostatistics, University Hospital of Basel, University of Basel, Basel, Switzerland

<sup>3</sup> Proteomics Core Facility, Biozentrum, University of Basel, Basel, Switzerland

<sup>4</sup> Department of Neurosurgery, University Hospital Basel, and Brain Tumor Immuno-Therapy and Biology Laboratory, Department of Biomedicine, University Hospital of Basel, University of Basel, Basel, Switzerland

**Aims:** Glioma are currently classified according to integrated histopathologic and molecular genetic (WHO 2021 classification) as well as methylomic criteria (Capper 2018). However, little is known about proteomic profiling of these subgroups, which may reveal specific biomarkers and pathways potentially activated or inactivated.

**Methods:** Eighty-six glioma biopsy samples were prospectively collected from patients undergoing surgery at the University Hospital of Basel between 2017 and 2019. Samples were classified into seven distinct glioma subgroups based on integrated WHO 2016 and methylome profiling criteria. Proteins were extracted from fresh frozen samples devoid of necrosis/haemorrhage and processed for mass spectrometry analysis.

**Results:** For each tumour sample, a total of 8855 proteins were identified and quantified. 950 proteins were differentially expressed between at least two glioma subgroups. Strikingly, most significant differences in expression are related to tumor grading rather than to glioma subgroups.

Proteins SSDH and GABT, involved in Gamma-aminobutyric acid (GABA) catabolism, show the strongest increase between low grade glioma (LGG) and high grade glioma (HGG), whereas S10AA and ANXA2, part of pathways involved in coagulation, cell adhesion and immune response, appear increased in HGG.

**Conclusions:** Tumor grading turns out to be dominant over genetic and epigenetic criteria for proteomic classification. Most significant protein level variations may represent potential glioma grade-specific therapeutic targets.

P083

### Intraoperative Motor Evoked Responses to Double-Train Paradigm Stimulation for Guiding Lead Placement and Postoperative Programming in Spinal Cord Stimulation for Pain

J. A. Schlaeppli <sup>1</sup>, R. Schreen <sup>2</sup>, R. Mija <sup>2</sup>, A. Nowacki <sup>2</sup>, C. Pollo <sup>2</sup> and K. Seidel <sup>2</sup>

<sup>1</sup> Inselspital, Bern University Hospital, University of Bern, Switzerland

<sup>2</sup> Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland

**Objective:** To demonstrate the feasibility of using motor evoked responses to intraoperative double-train stimulation to guide lead placement and matching of intraoperative contacts with postoperative electrode programming in spinal cord stimulation for pain performed under general anesthesia.

**Materials and Methods:** The study included a series of 20 consecutive patients with refractory pain. Either percutaneous or paddle leads were implanted and positioned according to the intraoperative mapping results. Neurophysiologic mapping was performed with a double-train stimulation paradigm. The sites where dorsal column responses of the targeted dermatomes were detected were considered optimal for lead placement. Following spinal cord stimulator (SCS) lead placement, blinded postoperative programming of electrode contacts was matched with the intraoperative best contacts and the pain-paresthesia overlap for the trial phase. A binominal test was used as a statistical method; pre- and postoperative numeric rating scale (NRS) after three months was obtained.

**Results:** A total of 15 patients underwent spinal cord stimulation trial for intractable pain. Of these, ten patients (66%) had a successful trial and received permanent implants; one patient had a successful trial but was never intended to be implanted because of her poor health condition; four patients (26%) had an unsuccessful trial, leading to trial electrode explantation; and five patients had already had an implant with percutaneous leads and therefore underwent electrode revision, of whom four patients received paddle leads. In 18 of the 20 operated patients (90%), we found a match between the best intraoperative contacts and the postoperatively programmed contacts (significantly better than chance,  $p = 8.2 \times 10^{-15}$ ). In 90% of the patients, a pain-paresthesia overlap of 100% was found. In the remaining two patients (10%), the postoperatively best programmed contacts were one contact away from the intraoperative neurophysiologic best contact. A mean preoperative NRS score of 8.2 (variance) and a mean follow-up NRS score after three months of 3.6 (variance) were obtained for all patients with implants.

**Conclusions:** In this study, we were able to demonstrate that SCS lead placement using a double-train stimulation paradigm performed under general anesthesia is a safe and feasible technique, offering reliable prediction of contacts for postoperative programming and excellent pain-paresthesia coverage.

P084

## Deep Learning Approach for Differentiation between Glioblastoma and CNS Lymphoma Using Gramian Angular Field

A. Hakim <sup>1</sup>, I. Zubak <sup>2</sup>, T. Rhomberg <sup>2</sup>, J. Slotboom <sup>1</sup> and M. Murek <sup>2</sup>

<sup>1</sup> Department of Neuroradiology, Inselspital, Bern University Hospital, University of Bern, Switzerland

<sup>2</sup> Department of Neurosurgery, Inselspital, Bern University Hospital, University of Bern, Switzerland

**Aim:** Differentiating between glioblastoma (GBM) and lymphoma is of utmost importance for treatment planning. Due to the overlap in imaging features between the two entities, advanced imaging including spectroscopy is an adjunct that helps in the differentiation. However, there are limitations regarding training a network using one-dimensional data with deep learning. We aim to evaluate the possibility of converting the one-dimensional spectrum data into a two-dimensional image using gramian angular field to be used as input for a convolutional neural network for the differentiation between GBM and lymphoma.

**Method:** Data from patients with GBM or lymphoma who underwent preoperative MR spectroscopy in Inselspital Bern was collected. Operative cases with proven histopathology acted as the reference standard. Two different spectra data were used separately and at the end, the performance was compared; (1) the signal curve obtained directly from the MR scanner and (2) the fitted curve obtained during the standard post-

processing of spectroscopy. Both curves were converted separately into images using gramian angular summation field, and the images obtained were used as the input for a neural network. The prediction results were compared between data obtained from the signal curve and the whole fit curve.

**Results:** The final number of patients fulfilling the inclusion criteria was 98 (65 GBM, and 33 lymphomas). Of these, 20% (19 cases, 14 GBM, and 5 lymphomas) were used for testing the algorithm. The prediction on the training pathway using signal curves performed better than the pathway using the whole fit curve. The overall accuracy of the prediction from the signal curve was 73% and from the whole fit curve was 63%. The sensitivity for detecting glioblastoma was 0.92 on the signal pathway compared to 0.79 on the whole fit pathway. The false-negative rate was also better on the pathway using the signal curve with 0.08 compared to the whole fit pathway with 0.21.

**Conclusions:** Spectroscopy data can be converted into an image using gramian angular field which allows for the utilization as input for a deep learning network. Differentiation between GBM and lymphoma using this method achieves good accuracy, which is better when data originates from the signal curve, compared to the whole fit curve.

P085

### Evolution of Head Injuries in Downhill Skiing over 30 Years: Are Helmets Really Doing the Job?

J. Fournier <sup>1</sup>, A. Simonin <sup>2</sup>, D. Pioletti <sup>3</sup>, K. Papadimitriou <sup>1</sup> and D. Kiss-Bodolay <sup>4</sup>

<sup>1</sup> Hôpital du Valais (HVS)—Centre Hospitalier du Valais Romand, Switzerland

<sup>2</sup> Hôpital du Valais—Sion

<sup>3</sup> EPFL

<sup>4</sup> HUG Switzerland

Evolution of head injuries in downhill skiing over 30 years: are helmets really doing the job?

**Background:** Head injury accounts for 3–15% of winter sport-related injuries but remains the leading cause of death and severe disability among skiers and snowboarders. In spite of the generalized use of ski helmets that was associated with a decrease in scalp wounds and skull fractures there seems to be a paradoxical increase in severe brain injuries as compared to the pre helmet areas, raising the question of their efficiency.

**Methods:** We compared two case-series of winter sports related traumatic head injuries from 11 winter seasons between February 1981 and April 1993 with the 2020 winter season aborted by the COVID-19 pandemic. All the data analyzed comes from a single institution (Sion Cantonal Hospital, Switzerland). History, clinical presentation, radiological features, treatment and outcomes were collected retrospectively and compared between both case series.

**Results:** All the injured patients during the 2020 season wore helmet against none between 1981–1993. The incidence of skull fracture dropped significantly from 81% between 1981–1993 to 11% in 2020 and with it the incidence of brain contusion (49% between 1981–1993 to 11% in 2020) and death (38% between 1981–1993 to 5% in 2020). Strikingly however, the number of patients sustaining deceleration related diffuse axonal injury (DAI) increased by more than 5 folds (7% between 1981–1993 to 39% in 2020) with a poor outcome in 2/3 of the cases (cognitive impairments related to DAI in 5/7 cases) at the time of discharge from the hospital. This paradoxical increase is in accordance with 3 reported series. Among the DAI sustaining patients all except one were in the < 50 years old age group.

**Conclusions:** There is a clear paradoxical increase in DAI since the systematic use of helmets in downhill skiing, in accordance with the literature. This observation raises the following legitimate question: are helmets doing the job? This question motivated the senior author to join a research group from the ETH Lausanne in order to optimize

downhill ski helmets using modern simulation techniques as well as new materials. First findings of these researches will be presented.

P086

### Deep Brain Stimulation of the Central Lateral and Ventral Posterior Thalamus for Central Poststroke Pain Syndrome: Preliminary Experience

A. F. Nowacki <sup>1</sup>, D. Zhang <sup>2</sup>, J. Rosner <sup>3</sup>, M. Arnold <sup>4</sup> and C. Pollo <sup>4</sup>

<sup>1</sup> Inselspital, Switzerland

<sup>2</sup> Bern University Hospital, University Bern, Bern, Switzerland

<sup>3</sup> Bern University Hospital, Bern, Switzerland

<sup>4</sup> Bern University Hospital, Inselspital Bern, Switzerland

**Objective:** The beneficial effects of thalamic Deep Brain Stimulation (DBS) at various target sites to treat chronic central neuropathic pain (CPSP) remain unclear. The objective of the present study was to evaluate the effectiveness of DBS of previously untested target site in the Central lateral thalamus along with classical sensory thalamic stimulation.

**Methods:** This is a monocentric retrospective study of a consecutive series of six patients with CPSP who underwent combined DBS lead implantation of the central lateral (CL) and sensory thalamus (ventral posterior complex). Patient reported outcome measures were collected before and after surgery using the visual analog scale, McGill pain questionnaire, EQ-5D quality of life questionnaire and Beck depression index. DBS leads were reconstructed and projected onto a three-dimensional stereotactic atlas.

**Results:** VAS but not sf-MPQ pain intensity was significantly reduced throughout the follow-up period of 12 months compared to baseline ( $p = 0.005$ , and  $p = 0.06$  respectively, Friedman test). At last available follow-up (12 to 30 months), three patients described a more than 50% reduction. Two of the three long-term responders were stimulated in the MD/CL (1000 Hz, 90  $\mu$ s, 3.5–5.0 mA) while the other one preferred VP complex stimulation (50 Hz, 200  $\mu$ s, 0.7–1.2 mA). We did not notice any procedure or stimulation-associated persisting side-effects.

**Conclusions:** These preliminary findings suggest that DBS of the CL might constitute a potential alternative target in cases where classical VP complex stimulation does not yield satisfactory postoperative pain reduction. The results need to be confirmed in larger, prospective series of patients.

P087

### Blended Learning in Neurosurgical Resident Training—Course Development and Participant Evaluation

A. Hickmann, A. Ferrari, O. Bozinov, M. N. Stienen, C. Ostendorp

Kantonsspital St. Gallen, Switzerland

**Aims:** Training opportunities for surgical residents in the operating room (OR) are increasingly limited by working time restrictions, constraints in healthcare expenses and increasing sub-specialization with case load requirements per surgeon as well as increasing quality of care expectations. Nonetheless, surgical training requires goal-oriented and focused practice. To overcome these limitations trainings outside the OR are increasingly utilized. We have designed a two-step blended course consisting of a personalized adaptive e-learning module followed by a simulator training. We report on our experience with course development and first participants' evaluation.

**Methods:** Learning engineers designed the adaptive e-learning (Area-9 Lyceum) based on theoretical information provided by clinicians (subject matter experts). For the simulator training a lumbar spine model for image-guided spinal injections (3B scientific) was used.



Trainees were assigned to the e-learning module first and after its completion participated in the simulator training. To personalize the learning experience to the individual knowledge and needs, performance data was recorded for each participant's e-learning module. Simulator training was organized in small groups with a 1:4 instructor-participant ratio. Structured assessments were conducted adapted from the Student Evaluation of Educational Quality (SEEQ).

**Results:** The adaptive e-learning module was designed, reviewed and signed off within 10 weeks. To date, eight participants have taken the course. The overall rating of the course is "very good" (4.8/5). Adaptive e-learning is well received compared with other e-learning (8/10), but scores lower regarding "usefulness", "efficiency" and "fun" compared with the simulator training. Conscious competency ( $32.6 \pm 15.1\%$ ) improved and subconscious incompetency decreased ( $22.8 \pm 10.2\%$ ). The subjective skills level improved by 20%. Asked about the impact of the course, participants indicated that they had either learned something new that they plan to use in their practice (71.4%) or felt reconfirmed in their practice (28.6%).

**Conclusions:** Developing a blended training course combining adaptive e-Learning and simulator training in a rapid manner is feasible and leads to improved skills. Simulator training is rated more valuable by surgical trainees than the e-Learning. The impact on patient care and optimal timing for taking the course need to be investigated further.

P088

### Intraoperative Neurophysiological Monitoring during Spinal Cord Stimulation Surgery: A Systematic Review

J. A. Schlaeppli <sup>1</sup>, R. Schreen <sup>2</sup>, K. Seidel <sup>2</sup> and C. Pollo <sup>2</sup>

<sup>1</sup> Inselspital, Bern University Hospital, University of Bern, Switzerland

<sup>2</sup> Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland

**Aim:** To describe the state of literature regarding the use of intraoperative neurophysiological monitoring (IONM) during spinal cord stimulator surgery.

**Methods:** A systematic review of the use of IONM during spinal cord stimulation (SCS) surgery was performed using the following three Databases: PubMed, Ovid Medline and Embase. Research techniques included systematic research following the PRISMA Protocol by Cochrane and backward searching. Qualitative analysis of included papers was performed using the MINORS assessment Tool. Direction of effect, consistency across studies and cost-effectiveness were narratively synthesized.

**Results:** A total of 14 records were identified through database searching. All records used neuromonitoring methods under general anesthesia for guidance of epidural lead placement. IONM techniques used for determining lateralization in the found papers were compound muscle action potentials (CMAP,  $n = 7$ ), somatosensory evoked potentials (SSEP,  $n = 3$ ) or both ( $n = 4$ ). Motor evoked potentials (MEP) were used in three trials for neuroprotection purposes. Two studies were comparative and twelve were non-comparative.

**Conclusions:** We found a good body of level II evidence 1 that the use of IONM during spinal cord stimulation surgery is a valid alternative to awake surgery and may even be superior regarding pain management, cost-effectiveness and postoperative neurological deficits. We state a B degree of recommendation 1 for performing SCS lead placement under general anesthesia with the use of IONM. In direct comparison, the found evidence suggesting compound muscle action potentials proving more consistent favorable results than the use of somatosensory evoked potentials for midline placement of epidural leads under general anesthesia. Selection of IONM modality should be made based on pathophysiology of disease, personal electrophysiological experience and the individual patient.

P089

## Does Cortical Spreading Depolarization affect the Autonomous System Regulation Measured by Heart Rate Variability Changes

N. Tahhan <sup>1</sup>, M. Berhouma <sup>1</sup>, A. Meiller <sup>2</sup>, J. Dreier <sup>3</sup>, E. Kang <sup>4</sup>, C. Lemale <sup>4</sup>, S. Marinesco <sup>2</sup> and B. Balanca <sup>1</sup>

<sup>1</sup> Hospices Civils de Lyon, France

<sup>2</sup> Lyon Neuroscience research Centre, France

<sup>3</sup> Department of Neurology, Charité–Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Germany

<sup>4</sup> Charite—Universitaetsmedizin Berlin, Germany

**Introduction:** Spreading depolarization (SD) are now considered as a hallmark of all acute brain injuries. They propagate from an injured area through the neighboring cortical matter and can cause cell swelling and injury. SD is a marker of poor prognosis and delayed injury progression, and the mechanism by which SD affects the outcome is multifactorial. Whether SD invades subcortical areas and may alter brainstem functions such as autonomous regulation is still controversial. Our hypothesis was that the type of anesthetic agent changes the way SD affects the autonomous regulation.

**Materials and Methods:** We conducted a retrospective analysis of animal data collected in different experiments studying SDs in adult male Wistar Kyoto rats under general anesthesia with Isoflurane, Propofol or Thiopental. Animals were artificially ventilated, and their temperature was kept at 38°C with a heating pad. Their heart rate was monitored with a femoral arterial line or ECG electrodes. SDs were triggered by a cortical application of KCl and recorded with a local field potential electrode connected to a DC amplifier. We computed heart rate variability analyses with the Neurokit 2 library in Python 3.8. The changes observed before, during and after SD were analyzed using the R software with a linear regression mixed effect model. Data are expressed by their median and interquartile range (median [25–75th]). Quantitative data were compared with the paired Wilcoxon rank sum test using a Bonferroni correction for multiple analyses.

**Results:** We included 21 male animals (Isoflurane:  $n = 9$ , propofol:  $n = 9$ , and Thiopental:  $n = 7$ ). The median of the mean RR interval was significantly lower under isoflurane (142.299 ms [135.19–150.445]) compared to thiopental (165.21 [152.501–170.34],  $p = 0.044$ ) but not propofol (163.706 ms [151.153–176.155],  $p = 0.28$ ). The RR interval standard deviation was also lower with isoflurane (1.506 ms [1.434–1.729]) compared to thiopental (5.825 [5.051–8.078],  $p = 0.03$ ) but not propofol (2.886 [2.018–5.996],  $p = 0.27$ ).

The standard deviation of the RR interval was significantly higher during SD ( $p = 0.037$ ), and the mean RR interval change after SD was different between isoflurane and thiopental ( $p = 0.027$ ).

**Conclusions:** SD can have different consequences on the brain stem functions such as the autonomous regulation depending on the anesthetic agent.

P090

## Long Term Cosmetic, Ophthalmological, Cognitive, and Parental Satisfactory Outcome after Open Sagittal Craniosynostosis Repair

S. M. Pinar <sup>1</sup>, T. J. Hallenberger <sup>2</sup>, M. Licci <sup>3</sup>, B. K. Benitez <sup>4</sup>, A. Palmowski-Wolfe <sup>5</sup>, F. Roulez <sup>5</sup>, R. Guzman <sup>2</sup> and J. Soleman <sup>2</sup>

<sup>1</sup> Faculty of Medicine, University of Basel, Switzerland

<sup>2</sup> Department of Neurosurgery, University Hospital of Basel, Switzerland

<sup>3</sup> Department of Pediatric Neurosurgery, University Children's Hospital of Basel, Switzerland

<sup>4</sup> Department of Oral and Craniomaxillofacial Surgery, University Hospital of Basel, Switzerland

<sup>5</sup> Department of Ophthalmology, University Hospital of Basel, Switzerland

**Aim:** The aim of this study was to investigate the long-term cosmetic, ophthalmological, cognitive, and parental satisfactory outcome of children after open surgical correction for non-syndromic sagittal craniosynostosis.

**Methods:** Patients under the age of twelve months, who underwent surgical reconstruction with a follow up period of at least 3 years after surgery at the Department of Pediatric Neurosurgery, University Hospital of Basel were included in this single center study. The primary outcome was parent-reported satisfaction of the surgery (PRSS) assessed through a parental questionnaire. Secondary outcomes were neurocognitive development and health-related quality of life (HRQoL), measured using the Vineland Adaptive Behavior Score (VABS) and the KINDL® questionnaire, ophthalmological outcome, and cosmetic outcome based on 3D imaging of the patients.

**Results:** We included 26 children with a mean age of 7.67 months at surgery (15% girls). Based on PRSS 25% of the parents were satisfied and 75% very satisfied with the surgical outcome. VABS showed a mean of 104.52, corresponding to an overall age-adequate adaptive level. Children aged 4–6 showed a mean score of 79.76/100 for HRQoL, while children aged 7–13 showed a mean score of 76.04/100, which is within the norm. Cosmetic outcome based on 3D photos, and ophthalmological outcome will be presented as well.

**Conclusions:** Our preliminary results demonstrate, high parental satisfaction with the surgical repair of open sagittal synostosis. The patients do not seem to have more intellectual or developmental disabilities than the average of normal population while the HRQoL is within the norm.

P091

#### **Preliminary Results of a Two Saccular Elastase Digested Aneurysm Model in a Rabbit—A Technical Report**

**J. Kümmin**<sup>1</sup>, **G. Boillat**<sup>1</sup>, **S. Ulmer**<sup>2</sup>, **R. Schmied**<sup>2</sup>, **F. Tim**<sup>2</sup>, **S. Wanderer**<sup>1</sup>, **H. Widmer**<sup>3</sup>, **R. Luca**<sup>1</sup>, **L. Anderegg**<sup>1</sup>, **S. Marbacher**<sup>1</sup> and **G. Basil E.**<sup>1</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> Universität Bern, Switzerland

<sup>3</sup> Inselspital—Universitätsspital Bern, Switzerland

**Introduction:** Preclinical extracranial aneurysm models play a key role in research and understanding of the pathophysiological processes regarding healing mechanisms of human intracranial aneurysm (IA) as well as for testing novel endovascular devices. Models with hemodynamic, morphologic and histologic characteristics similar to human IAs are essential. Therefore, the aim of this study was to demonstrate the reproducibility of creating two experimental aneurysms with different hemodynamic and wall conditions in one animal.

**Methods:** 17 New Zealand white rabbits with a mean weight of 4 ( $\pm 0.3$ ) kg and mean age of 20 ( $\pm 5$ ) weeks underwent surgery with microsurgical creation of a bifurcation and stump aneurysm. Stump aneurysms were created at the origin of the right common carotid artery (CCA), bifurcation aneurysms sewn in an artificial created bifurcation between left and right CCA. Both aneurysms were treated with elastase. Patency was controlled by intraoperative fluorescence angiography. Intermediate patency rates were assessed four weeks postoperatively using MR-angiography. No anticoagulants were applied.

**Results:** All stump aneurysms showed a good intraoperative pulsation and perfusion in fluorescence angiography. Five of the bifurcation aneurysms showed partial thrombosis that resolved after flushing with heparinized saline in three of these aneurysms. One animal was lost to follow up due to anesthesiologic complications (pneumothorax). 16 animals (94.2%) reached the follow up four weeks after creation. All 16 stump aneurysms

were identified to be patent (100% patency rate). 3 of 16 bifurcation aneurysm had spontaneous thrombosis (81.3% patency rate).

**Conclusions:** The results demonstrate the reproducibility of the two-aneurysm model with good short and intermediate term patency rates of the stump and bifurcation aneurysm without administration of anticoagulants. Further testing and histological analysis are needed to confirm long-term patency rates and evaluate the course of aneurysm wall degeneration.

*P092-YouClin*

### **Severe Neuro-COVID Is Associated with Peripheral Immune Signatures and Signs of Neurodegeneration: A Prospective Cross-Sectional Study**

**M. M. Etter and G. Hutter**

Universität Basel & Universitätsspital Basel, Switzerland

**Aims:** To identify severity-dependent immune mechanisms in the cerebrospinal fluid (CSF) and plasma of COVID-19 patients and their association with brain imaging alterations. Also, associations of different protein secretion patterns and symptom severity with long-COVID were assessed.

**Methods:** We conducted a prospective cross-sectional study (EKNZ 2020-01503, NCT04472013), in COVID-19 patients during the ongoing pandemic (August 2020 to April 2021). We enrolled 40 patients which were prospectively assorted by neurological symptom severity into Neuro-COVID classes I (n = 18), II (n = 7) and class III (n = 15). Study interventions included cMRI or cCT, lumbar puncture, and blood withdrawal. Age and sex matched inflammatory neurological disorder patients (n = 25) and healthy individuals (n = 25) served as controls. 184 CSF and plasma soluble proteins were measured using proximity extension assays, and associated with Neuro-COVID severity. Further, the association of regional brain volumes with plasma and CSF parameters was assessed. CSF and plasma antibody profiles were analysed to identify possible autoantibodies in COVID-19 patients. To investigate the evidence of long-COVID, a 10-months follow-up was performed.

**Results:** COVID-19 patients (n = 40, mean [SD] age, 54 [20] years; 17 women (42%)) displayed a plasma cytokine storm but a non-inflammatory CSF profile. Class III patients displayed signs of blood-brain barrier (BBB) impairment and a polyclonal B cell response targeting self- and non-self antigens. Further, signs of microglia activation were more prevalent in these patients. We identified 16 specific brain regions that were negatively correlated to the CSF leukocyte count, protein levels and the CSF/plasma albumin ratio ( $p < 0.05$ ). Thereof, 81% corresponded to the olfactory and gustatory cortex's telencephalic connections. In the 10 months follow-up, Long-COVID was more prevalent in class III patients than in class I and II patients. Furthermore, we identified different CSF and plasma proteins predictive for long-COVID. Amongst others, high plasma levels of CLM-6 and MCP-3, high IFN-gamma and low TRANCE CSF levels.

**Conclusions:** Neuro-COVID class III patients had a strong, peripheral immune response, resulting in (1) BBB impairment (2) ingress of (auto-)antibodies, (3) and neuronal damage signatures, associated with long-COVID. Our data point towards several potentially actionable targets that may be addressed to prevent COVID-19-related neurological sequelae.

P093

### Polarimetric Visualization of Healthy Brain Fiber Tracts for Tumor Delineation during Neurosurgery (HORA0)

O. Rodríguez-Núñez <sup>1</sup>, L. Felger <sup>1</sup>, E. Hower <sup>2</sup>, T. Maragkou <sup>3</sup>, R. Mckinley <sup>4</sup>, M. Murek <sup>1</sup>, T. Novikova <sup>5</sup>, A. Pierangelo <sup>5</sup>, I. Zubak <sup>1</sup> and P. Schucht <sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Inselspital, Bern University Hospital, University of Bern, 3010, Bern, Switzerland

<sup>2</sup> Lausanne University Hospital and University of Lausanne, Switzerland

<sup>3</sup> Institute of Pathology, University of Bern, 3010, Bern Switzerland

<sup>4</sup> Support Center for Advanced Neuroimaging (SCAN), University Institute of Diagnostic and Interventional Radiology, University of Bern, Inselspital, Bern University Hospital, 3010, Switzerland

<sup>5</sup> LPICM, CNRS, Ecole polytechnique, IP Paris, Palaiseau, 91128, France

**Aims:** To identify the border of solid tumor remains a main challenge in glioma surgery. Difficulties in exact delineation of glioma are the risk factors for both reduced survival rate and neurological deficits. We explore the imaging Mueller polarimetry (IMP) for the visualization of fiber tracts of healthy brain by measuring the optical anisotropy and scattering properties of brain tissue. Seeing fiber tracts during brain surgery would enable us to delineate tumors (no fiber tracts) and to identify the tracts in sight based on their orientation for safe and complete brain tumor resection.

**Methods:** We implemented a wide-field visible wavelength IMP system to visualize the white matter fiber tracts using maps of depolarization, scalar retardance and azimuth of optical axis (polarimetric markers). The instrument is composed of an incoherent white light source, followed by the polarization state generator for polarization modulation of the incident light beam illuminating the sample. Light reflected or scattered by a sample is collected in the detection arm that includes the polarization state analyzer, followed by the spectral filters and a focusing system to generate the image on the camera.

Using the IMP system we recorded 16 intensity images for each brain tissue sample. The  $4 \times 4$  Mueller matrix (MM) images of three thick coronal sections of fresh calf brain, formalin-fixed calf brain and formalin-fixed human brain were reconstructed from the raw intensity images using eigenvalue calibration method. The maps of polarimetric markers were obtained by applying Lu-Chipman decomposition algorithm pixel-wise to the experimental MMs.

**Results:** The acquired in-plane polarimetric images showed that for both formalin-fixed and fresh brain section, the values of scalar linear retardance and depolarization in cerebral white matter are higher compared to the corresponding values in gray matter. In addition, it was possible to visualize the orientation of the white matter fiber tracts in sight using azimuthal maps of the optical axis.

**Conclusions:** Our results demonstrate that for the three sections of coronal brain tissue, the presence and direction of white matter fiber tracts are clearly detectable using polarimetric markers. The results of our proof-of-concept studies prove the potential of wide-field IMP that offers a fast, reproducible, stain-free, non-invasive method to identify tumor margins indirectly by detecting white matter fiber tracts during brain surgery.

P094

### Path to Success: Women Leaders in German Neurosurgery

M. Weiss <sup>1</sup>, U. Eisenberg <sup>2</sup>, A. Velalakan <sup>3</sup>, I. Moritz <sup>4</sup>, D. Nistor-Gallo <sup>5</sup>, C. Flüh <sup>6</sup>, S. Hernández Durán <sup>7</sup>, J. Krüger <sup>8</sup> and M. Forster <sup>9</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> Warthestrasse 70, Germany

<sup>3</sup> Neurochirurgisches Zentrum Ludwigsburg-Heilbronn, Germany

<sup>4</sup> Klinikum Berlin-Neukölln, Germany

<sup>5</sup> Universitätsklinikum Erlangen, Germany

<sup>6</sup> Universitätsklinikum Schleswig Holstein, Germany

<sup>7</sup> Universitätsklinikum Göttingen, Germany

<sup>8</sup> Ohlestrasse 44a, Germany

<sup>9</sup> Universitätsklinikum Frankfurt am Main, Germany

**Aims:** Advances in gender equality in medicine have been achieved worldwide. In Germany, almost 70% of medical students are female, and the proportion of board-certified physicians is approximately 60%. However, on the path to leadership positions, the proportion of women becomes progressively less, with female department chairs being a minority. This phenomenon is particularly true in surgical specialties, and neurosurgery is not an exception, with only 6% of department chairs being women. We aimed to characterize the career pathways of female chairs of neurosurgical departments in Germany.

**Methods:** We approached current and former female chairs in German neurosurgery and gathered descriptive information on their ways into leadership positions through structured interviews.

**Results:** Data were obtained from 15/19 (79.0%) female neurosurgical chairs who are all still alive and aged between 44–82 years. German female neurosurgical chairs completed their training within 6.5–0.5 years, and it took them further 13.7–4.5 years through the ranks between training completion and chair acquisition. Six female neurosurgical chairs had made working experiences or fellowship training abroad. Having obtained their chair positions between 1993 and 2020,  $n = 4$  of them have retired or changed career tracks. Of  $n = 11$  (73.3%) still practicing,  $n = 3$  (20.0%) are directors of university hospitals.  $N = 12$  (80.0%) hold professorships.  $N = 8$  (53.3%) spent time abroad for clinical education or research. Information on private life was obtained on  $n = 10$  (66.7%) German female neurosurgical chairs, with  $n = 7$  (46.7%) being married and  $n = 5$  (33.3%) having children.

**Conclusions:** This study provides information on the small number of German female neurosurgical chairs and their long and winding, obstacle-ridden paths to neurosurgical leadership positions. In future, these should become historical in order to perceive the presence of women in leadership positions no longer as an oddity, but as self-evident normality, reflecting our society. However, further analyses comparing paths of both German female and male neurosurgical chairs are necessary for highlighting women's difficulties on their way to neurosurgical leadership positions.

P095

## Endoscopic Evacuation of Acute Subdural Hematoma in the Elderly: A Double Case Report

E. Chaboudez. L. Weman. J. Fournier

Hôpital du Valais, Sion, Switzerland

**Background:** The standard surgery for acute subdural hematoma (aSDH) is a craniotomy/craniectomy with hematoma evacuation. This intervention is associated with a high mortality and morbidity in the elderly. Trepanation with two burr holes in case of chronic subdural hematoma has to the contrary proved to be well tolerated in the elderly. We describe two cases of endoscopic evacuation of aSDH through burr hole trepanation in two elderly patients.

**Cases:** The two patients were 77- and 80-year-old with voluminous acute subdural hematoma on CT scan. No other traumatic intracerebral lesions were associated. One presented with complete facio-brachio-cural hemiplegia with Glasgow Coma Scale (GCS) 14/15 and the other with loss of consciousness and a GCS of 6/15 without mydriasis. Both patients would have presented a high risk of mortality in case of a standard craniotomy

and evacuation. We chose to undergo a two-burr hole trepanation and evacuation with endoscopic view.

**Results:** We achieved a controlled and thorough evacuation of both aSDHs. The instruments could be visualized at every step of the procedures and the aSDH's cavities enabled a good visualization of the hematoma and cerebral parenchyma. The two patients recovered well and improved their preoperative neurological deficit and GCS score without any major complication. Both postoperative CT scan showed sufficient evacuation and reduction of mass effect and midline shift. Both interventions were done in a significantly shorter time than for a craniotomy.

**Discussion:** aSDH often presents a different pathophysiology in the elderly. They frequently occur in an acute on chronic setting with significantly lower trauma kinetic, less intracerebral lesion and cerebral edema. They commonly require a craniotomy for evacuation without a craniectomy. Older patients with cerebral atrophy also have more subdural space probably helping the endoscopic visualization. These factors make a minimally invasive endoscopic evacuation an interesting modality to treat this condition often associated with a high mortality.

**Conclusions:** Endoscopic evacuation of aSDH through two burr holes in elderly patients is likely an effective and safe alternative to a craniotomy, especially in patients without associated intracerebral lesions.

P096

### Neuromonitoring with Intraoperative 3 Tesla Magnetic Resonance Imaging in Neurosurgery: The Geneva Setup

L. A. Crowe <sup>1</sup>, C. Boëx <sup>2</sup>, P. Bijlenga <sup>1</sup>, O. Lorton <sup>1</sup>, M. Vargas <sup>1</sup>, N. Bérard <sup>3</sup>, J. Vallée <sup>1</sup>, K. Schaller <sup>1</sup> and R. Salomir <sup>1</sup>

<sup>1</sup> HUG Hôpitaux Universitaires Genève, Switzerland

<sup>2</sup> University Hospitals of Geneva, Switzerland

<sup>3</sup> CHUV—Hôpital universitaire, Switzerland

**Aims:** The life expectancy following the surgeries of gliomas, has been shown to be longer with extensive lesion resection. This knowledge motivated the development of intraoperative magnetic imaging scanning (MRI) with the purpose to control the completeness of the resection. Life expectancy is also linked to the quality of like after cerebral lesion resection. The possibility to prevent lesion of so-called “eloquent” cerebral substrates, were developed in particular for the corticospinal tract. A technical progress can only be one if it does not prevent from using a mandatory modality of safe practice. In this context, technical solutions have been searched for integrating intraoperative monitoring to neurosurgical cases performed with intraoperative MRI. The objective of the study was first to develop a safe neuromonitoring setting in the 3T MRI. Preliminary tests and measurements were undertaken for adapting electrodes and wires of the neuromonitoring for safe MR and high-quality scanning.

**Methods:** The dedicated subdermal platinum-iridium (Pt-Ir) needle electrodes were here shortened in regard to their initial length (Dias et al., 2018). For limiting induced electrical signals in their wires, care was specially attended to prevent any loop and wire crossing. In addition they were all placed as most as possible at the site of the scan axis.

**Results:** A series of preoperative testing, performed with patch test in a volunteer with ex vivo muscle, was performed for identifying safe needle electrode length. With total electrode length of 1360 mm, MR scans using SAR limited to 60%, i.e., 1.2 W/kg, were determined as safe.

The first series of patients operated with that neuromonitoring setting with intraoperative 3T MRI in Geneva will be described (CE 2022-00566). The electrodes used did not

deteriorate the quality of the MRI images. No redness at the point of placement of the electrodes was observed.

**Conclusions:** We could identify an installation setup for safe intraoperative 3T MRI with neuromonitoring. Scalp electrode length and position were determined for safe scanning with electrodes staying in place, they were then introduced for standard clinical use.

P097

### Introduction of the Scentroid Intraoperative Olfactometer for Intraoperative Neuromonitoring of Olfaction

C. Boëx <sup>1</sup>, N. Bérard <sup>2</sup>, R. Tyrand <sup>3</sup>, S. Momjian <sup>3</sup> and K. Schaller <sup>3</sup>

<sup>1</sup> University Hospitals of Geneva, Switzerland

<sup>2</sup> CHUV – Hôpital universitaire, Switzerland

<sup>3</sup> HUG Hôpitaux Universitaires Genève, Switzerland

**Aims:** The objective of the study was to introduce intraoperative monitoring of olfaction. Here we introduce a new olfactometer specially designed for intraoperative use: the Scentroid system SE700 (Ontario, Canada).

**Methods:** We report olfactory evoked potentials performed with 7 normosmic volunteers (5 female, 2 male; CE 14-076). Evoked potentials were obtained for H<sub>2</sub>S stimuli (6.9 ppm; 8 l/m; 200 ms; 60% humidity; 32°C); computed over at least 70 epochs (0.5–100 Hz; artefact rejection criterion 45 µV)

**Results:** Standard fronto-temporal N1 responses, ipsilateral to the stimulated nostril, were observed in this series of volunteers. This response waveform having been shown to be measurable under general anesthesia, it will be used for intraoperative monitoring of olfaction.

**Conclusions:** The first patients operated with monitoring of olfaction using the Scentroid system are expected in the coming months in the Neurosurgery Department of the University Hospitals of Geneva.

P098

### Optimal Timing and Functional Outcome of Ventriculoperitoneal Shunt Placement in Hydrocephalus after Aneurysmal Subarachnoid Hemorrhage

J. Jost, A. Tortora, S. Marbacher, C. Musahl, G. Schubert, B. Grüter, L. Anderegg and S. Wanderer

Kantonsspital Aarau, Switzerland

**Aims:** Shunt-dependent chronic hydrocephalus (HC) is a common sequela in patients with aneurysmal subarachnoid hemorrhage (ASAH). However, there is still poor evidence as to the optimal timing of ventriculoperitoneal shunt (VPS) placement, particularly in the context of early complications such as delayed cerebral vasospasm (DCV) potentially associated with delayed cerebral ischemia. The purpose of this study was to compare the impact of early (<21 d after ASAH) vs. late VPS placement (≥21 d after ASAH) on functional clinical outcome in patients with HC after ASAH.

**Methods:** Data from 97 patients requiring VPS placement after ASAH enrolled in our institutional database between 2011–2021 were identified and analyzed retrospectively. We compared 2 groups, early VPS placement (<21 days after ASAH) vs. late VPS placement (≥21 days after ASAH), regarding demographics, ASAH grading, radiological parameters (Evans' index and BNI), impact and complications of externalized CSF drains, DCV, VPS associated complications and neurological functional outcome

**Results:** 64 patients with early and 33 with late VPS implantation were identified. Mean follow-up included 34.6 ± 29.5 months in the early and 43.3 ± 37.9 months in the late



group ( $p = 0.33$ ). Preoperative mRS (early  $3.14 \pm 1.2$ /late  $3.42 \pm 1.15$ ,  $p = 0.28$ ), GOS (early  $3.4 \pm 0.66$ /late  $3.2 \pm 0.54$ ,  $p = 0.2$ ) and eGOS (early  $4.7 \pm 1.5$ /late  $4.4 \pm 1.5$ ,  $p = 0.43$ ) were not different in both groups. Postoperative mRS (early  $1.28 \pm 1.2$ /late  $2.18 \pm 1.38$ ,  $p = 0.0015$ ), GOS (early  $4.5 \pm 0.67$ /late  $3.9 \pm 0.88$ ,  $p = 0.001$ ) and eGOS (early  $6.8 \pm 1.4$ /late  $5.8 \pm 1.7$ ,  $p = 0.0026$ ) showed significantly better functional results in patients with early CSF diversion. The rate of asymptomatic DCV did not differ significantly between both groups (early 43.75% ( $n = 28$ )/late 45.45% ( $n = 15$ ),  $p = 0.89$ ), neither for symptomatic CVS (early 46.85% ( $n = 30$ )/late group 57.57% ( $n = 19$ ),  $p = 0.54$ ). There was no difference in the rate of VPS placement associated complications (early 23% ( $n = 15$ )/late 33% ( $n = 11$ ),  $p = 0.43$ ) or overall mortality (early 11% ( $n = 7$ )/late 6% ( $n = 2$ ),  $p = 0.35$ ) in both groups.

**Conclusions:** Early VPS placement after ASAH in patients is feasible and safe. In our retrospective series it was associated with better functional short and long-term outcomes than late shunt implantation. Based on these data, early shunt implantation (<21 d after ASAH) might not be harmful in patients developing HC after ASAH.

P099

### Risk Assessment of Intracranial Aneurysm Remnants after Microsurgical Clipping Based on 3D-Digital Subtraction Angiography

B. Grüter <sup>1</sup>, L. Anderegg <sup>1</sup>, P. Gruber <sup>1</sup>, S. Wanderer <sup>1</sup>, P. Trost <sup>1</sup>, J. Berberat <sup>1</sup>, H. Steiger <sup>1</sup>, C. Marco <sup>2</sup>, G. A. Schubert <sup>1</sup>, L. Remonda <sup>1</sup> and S. Marbacher <sup>1</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> Universität Basel, Switzerland

**Background:** Several factors (such as i.e., intracranial aneurysm (IA) size, location, rupture status, shape, or use of multiple clips) have been suggested to predict the risk of incomplete IA clipping. However, their assessment has been based on 2D- digital subtraction angiography (2D-DSA), which fails to detect >30% of remnants detected on 3D-DSA.

**Objectives:** We aimed to identify risk factors for IA remnants after microsurgical clipping based on 3D-DSA imaging.

**Methods:** A consecutive series of 329 clipped IAs in 305 patients with 3D-DSA analyse immediately after clipping was evaluated for the presence of IA remnants. Multivariate regression analyses were performed to assess for potential risk factors on the odds of remnant presence.

**Results:** After clipping of 329 IAs, 76 aneurysm remnants were present based on 3D-DSA. Pre-treatment IA size was the only robust risk factor identified to be associated with the presence of remnants ( $p < 0.001$ ). However, multivariate regression analysis found no association for IA rupture status (subarachnoid haemorrhage) ( $p = 0.237$ ), IA localization ( $p = 0.11$ ), use of multiple clips ( $p = 0.07$ ), broad based IAs ( $p = 0.38$ ), IA shape ( $p = 0.77$ ) or IA calcification ( $p = 0.97$ ).

**Conclusions:** When assessed by 3D-DSA, the incidence of IA remnants after clipping is higher than reported in the literature. In our series of 3D-DSA based imaging, initial IA size is a robust independent risk factor for incomplete clipping, and these cases have to be followed closely.

P100

### Natural History of Carotid Artery Free-Floating Thrombus—A Single Centre, Consecutive Cohort Analysis

M. Müller<sup>1</sup>, N. Raptis<sup>2</sup>, P. Mordasini<sup>1</sup>, W. Z'Graggen<sup>1</sup>, A. Raabe<sup>1</sup>, P. Schucht<sup>1</sup>, M. Heldner<sup>1</sup> and D. Bervini<sup>1</sup>

<sup>1</sup> Inselspital—Universitätsspital Bern, Switzerland

<sup>2</sup> Universitätsspital Basel, Switzerland

**Introduction:** Carotid free-floating thrombus (CFFT) is a rare cause of stroke and is thought to be associated with a high risk of recurrent cerebrovascular ischemic events. The existing data on the natural history and optimal treatment modalities of CFFT are scanty and no clear recommendations exist.

**Objective:** A retrospective analysis of a single-centre cohort of consecutive patients diagnosed with CFFT was conducted, investigating the risk for recurrent cerebrovascular events.

**Methods:** We performed a single-centre retrospective analysis including all patients presenting at our tertiary centre between January 2005 and December 2020 with symptoms consistent with ischaemic stroke and/or transient ischaemic attack. Digital subtraction angiography (DSA), computed tomography angiography (CTA) or magnetic resonance angiography (MRA) were used to diagnose CFFT. In all included patients, CFFT was confirmed with a second imaging modality. CFFT was defined on imaging as a contrast-filling defect extending into the carotid lumen. We gathered information on vascular risk factors, diagnosis and follow-up methods, modality of treatment and neurological outcome. A survival analysis was performed assessing the risk for recurrent cerebrovascular events.

**Results:** In total, N = 62 patients presenting with symptomatic CFFT were included. Mean age was 68 years, 69% (43/62) of patients were male, 52% (32/62) current or previous smokers, 76% (47/62) suffered from arterial hypertension, 68% (42/62) from dyslipidaemia, and 31% (19/62) from diabetes mellitus. Overall, 71% (44/62) of patients received any kind of intervention (endovascular or surgical carotid thrombo-endarterectomy [CEA]) at any time point during follow-up. 16% of patients (10/62) received intervention within 48 h after diagnosis of CFFT. The survival analysis and Kaplan-Meier model censoring patients at the time of intervention or last follow-up showed that the risk for any recurrent stroke was 19.7% within the first 7 days and 27.4% within 3 months after diagnosis. No patients experienced a new ischaemic stroke beyond 11 days after diagnosis of CFFT (n = 17, Figure 1).

**Conclusions:** The risk of recurrent ischemic events in patients with CFFT is high, especially in the first week after diagnosis. Prospective studies are needed to further investigate the optimal management of these patients.

P101

### Machine Learning for White Matter Fibre Tract Visualization in the Human Brain via Mueller Matrix Polarimetric Data

R. McKinley<sup>1</sup>, L. Felger<sup>2</sup>, E. Hewer<sup>3</sup>, T. Maragkou<sup>4</sup>, M. Murek<sup>2</sup>, T. Novikova<sup>5</sup>, O. Rodríguez-Núñez<sup>2</sup>, A. Pierangelo<sup>5</sup> and P. Schucht<sup>2</sup>

<sup>1</sup> Inselspital, Universitätsspital Bern, Switzerland

<sup>2</sup> Inselspital—Universitätsspital Bern, Switzerland

<sup>3</sup> CHUV—Hôpital universitaire, Switzerland

<sup>4</sup> University of Bern, Switzerland

<sup>5</sup> Ecole Polytechnique, Institut Polytechnique de Paris, France

**Aims:** A clear identification of the border between a brain tumor and surrounding healthy tissue during neurosurgery is essential in order to maximize tumor resection while preserving neurological function. However, tumor tissue is often difficult to differentiate from infiltrated brain during surgery. Most existing techniques have drawbacks in terms of cost, measurement time and accuracy. The fibre tracts of healthy brain white matter are composed of densely packed bundles of myelinated axons that form uniaxial linear birefringent medium with the optical axis oriented along the direction of the fibre bundle. Brain tumors, whose cells grow in a largely chaotic way, lack this anisotropy of refractive index. Therefore tumor tissue can be distinguished from healthy white matter using polarized light.

**Methods:** A wide-field visible wavelength imaging Mueller polarimetric system was used for the study of formalin-fixed human brain sections measured in reflection geometry. The non-linear decomposition of the Mueller matrices provided the maps of depolarization, scalar retardance and azimuth of the optical axis. We studied the effectiveness of machine learning methods (Deep learning Unet, logistic regression) for distinguishing grey and white matter using polarimetric data.

**Results:** Manually labelled polarimetric data was used to train a convolutional neural network and a logistic regression model to identify white matter. The Unet achieved a much higher discrimination of white and grey matter (AUC of 0.92) than logistic regression (AUC of 0.81). Within the identified white matter, surface fibre tracts could be visualized and tracked without disturbance from spurious signals in the grey matter.

**Conclusions:** We expect that Mueller polarimetric imaging modality combined with our ML algorithms for fibre tracking will visualize the directions of fibre tracts in imaging plane during tumor surgery, thus, allowing a neurosurgeon to orient himself, to spare essential fibre tracts and to make surgery more complete and safe.

P102

### The Relevance of Biologically Effective Dose and Irradiation Time for Hearing Preservation after Radiosurgery for Vestibular Schwannomas: A Retrospective Longitudinal Study

C. Tuleasca <sup>1</sup>, D. Starnoni <sup>2</sup>, S. Duroux <sup>3</sup>, M. George <sup>2</sup>, R. Maire <sup>4</sup>, R. T. Daniel <sup>2</sup>, D. Patin <sup>2</sup>, L. Schiappacasse <sup>2</sup>, M. Faouzi <sup>5</sup> and M. Levivier <sup>2</sup>

<sup>1</sup> CHUV Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland

<sup>2</sup> Lausanne University Hospital (CHUV), Switzerland

<sup>3</sup> Hôpital de Valais, Switzerland

<sup>4</sup> Lausanne University Hospital (CHUV), Switzerland

<sup>5</sup> Unisanté Lausanne, Switzerland

**Introduction:** Stereotactic radiosurgery (SRS) has become a common treatment approach for small-to-medium size vestibular schwannomas (VS).

**Methods:** Here, we evaluate the relationship between time (beam-on and treatment), biologically effective dose (BED) and the risk of hearing decline after SRS for VS in patients with Gardner Robertson (GR) classes I and II at baseline. This retrospective longitudinal study included 213 patients with useful baseline hearing treated between June 2010 and December 2019. The risk of passing from GR classes I and II to other classes III, IV and V and the increase in pure tone average (PTA, continuous outcome) were evaluated using a mixed-effect regression model.

**Results:** Binary outcome analysis revealed sex, dose rate, integral dose, time [beam-on time Odd's ratio OR 1.03,  $p = 0.03$ , 95% confidence interval CI 1.00–1.06, treatment time (same as for beam-on time OR 0.85,  $p = 0.02$ , CI 0.74–0.98)] and BED [calculated with beam-on time (OR 0.85,  $p = 0.02$ , CI 0.74–0.98)], as statistically significant. Fitted multivariable model included the sex (OR 6.39,  $p = 0.01$ , CI 1.40–29.09), dose rate (OR 7.28,  $p = 0.004$ , CI 1.91–27.72) and BED (calculated with beam-on time OR 0.77,  $p = 0.01$  and 95% CI 0.63–

0.94). Continuous outcome (PTA) analysis revealed age, integral dose received by the tumor, number of isocenters, time (beam-on time OR 0.20,  $p = 0.001$ , 95% CI 0.083–0.33) and BED (OR  $-0.97$ ,  $p = 0.001$ , 95% CI  $-1.54$ – $-0.40$ ), as statistically significant. Fitted multivariable model include the age (OR 0.29,  $p = 0.001$ , 95% CI 0.12–0.47) and BED (OR  $-1.13$ ,  $p < 0.001$  and 95% CI  $-1.72$ – $-0.54$ ). The maximal dose received by the cochlea was not statistically significant.

**Conclusions:** The time factor in which a physical dose is delivered, as well as BED were statistically significant for the risk of hearing loss after SRS for VSs, both in terms of decline in GR class or as continuous PTA values (even greater effect). Our analysis showed that the risk of hearing decline (GR class) was associated with male sex, higher RDR (cut-off 2.5 Gy/min), higher integral dose received by the tumor, beam-on time more than 20 min and BED values between 60–68 Gy. Such findings will encourage a deeper analysis of these parameters in the future SRS treatment planning.

P103

### Direct Cochlear Nerve Stimulation Monitoring through Evoked Muscle Responses during Retrosigmoid Vestibular Schwannoma Resection Surgery: A Preliminary Report

S. Diaz <sup>1</sup>, G. Cossu <sup>2</sup>, R. Maduri <sup>3</sup>, C. Tuleasca <sup>2</sup>, M. George <sup>2</sup>, M. Messerer <sup>2</sup>, M. Levivier <sup>2</sup>, E. Pralong <sup>2</sup> and R. Daniel <sup>2</sup>

<sup>1</sup> CHUV Lausanne, Switzerland

<sup>2</sup> CHUV, Lausanne, Switzerland

<sup>3</sup> Genolier Spine Care Center, Switzerland

**Aims:** Cochlear nerve (CN) preservation during surgery for large vestibular schwannoma (VS) may be challenging. Brainstem auditory evoked potentials (BAEPs) and cochlear compound nerve action potentials (CNAPs) clearly showed their limitation during surgery. Techniques to stimulate directly the CN in large tumors is lacking in current surgical practice. The post-auricular muscle response (PAMR) is a large sound-evoked muscle action potential that is measured on the skin near the muscle behind the ear. These responses are of muscular origin and often much larger than the BAEPs. Their higher signal to noise ratio allows much less averaging to produce a stable waveform.

We report our preliminary results of a surgical cohort of large VS after direct electrical intra-operative CN stimulation and recording of the PAMR using the same electrodes positioned for the recording of BAEPs (Cz–A1/A2).

**Methods:** Scalp electrodes were positioned on Cz-A1 and Cz-A2 to record both cochlear evoked responses and BAEPs. Direct CN stimulation and triggered EMG recording were performed with a Prass probe monopolar electrode (stimulation frequency 1 Hz, pulse duration 200  $\mu$ s, pulse intensity from 0.1 up to 2 mA). Acquisition time was 100 ms and the stimulation was performed at the cisternal portion of the CN covering the tumor. BAEPs were recorded from Cz-A1 and Cz-A2 derivations by averaging 1000 responses after audio stimulations (clicks, 120 to 130 dB intensity, rarefaction, 10.1 Hz frequency).

**Results:** PAMR were recorded in all patients at the ipsilateral vertex-ear lobe scalp electrode and in 90% it was also observed in the contralateral electrode.

The optimal stimulation intensity was found to be 1 mA at 1 Hz, with a good cochlear response and an absent response from other nerves. At that intensity, the ipsilateral cochlear response had an initial peak at a mean latency of  $11.6 \pm 1.5$  ms with an average amplitude of  $14.4 \pm 5.4$   $\mu$ V. These cochlear responses were found to be reversibly abolished by the use of neuromuscular blockers. One patient experienced a significant improvement in his audition, while the others were stable.

**Conclusions:** PAMR stimulation during surgery allows the identification of the entire cisternal course of the CN without entering into the plane between the tumor capsule and

the nerve, thereby enabling functional preservation of neural function. This technique may be of great importance in patients where a planned subtotal resection is considered.

P104

### Optimal Cerebral Perfusion Pressure and Brain Tissue Oxygen in Aneurysmal Subarachnoid Hemorrhage

M. Weiss <sup>1</sup>, M. Megjhani <sup>2</sup>, J. Ford <sup>2</sup>, K. Terilli <sup>2</sup>, N. Kastenholz <sup>3</sup>, D. Nametz <sup>2</sup>, S. B. Kwon <sup>2</sup>, A. Velazquez <sup>2</sup>, S. Agarwal <sup>4</sup>, D. Roh <sup>4</sup>, C. Conzen-Dilger <sup>3</sup>, W. Albanna <sup>3</sup>, M. Veldeman <sup>3</sup>, E. S. Connolly Jr. <sup>4</sup>, J. Claassen <sup>4</sup>, M. Aries <sup>5</sup>, G. A. Schubert <sup>1</sup> and S. Park <sup>2</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> Columbia University, USA

<sup>3</sup> RWTH Aachen University, Germany

<sup>4</sup> Columbia University Irving Medical Center, USA

<sup>5</sup> Maastricht University Medical Center, Netherlands

**Aims:** Targeting a cerebral perfusion pressure optimal for cerebral autoregulation (CPPopt) has been gaining more attention to prevent secondary damage after acute neurological injury. Brain tissue oxygenation (PbtO<sub>2</sub>) can identify insufficient cerebral blood flow and secondary brain injury. Defining the relationship between CPPopt and PbtO<sub>2</sub> after aneurysmal subarachnoid hemorrhage (aSAH) may result in (1) mechanistic insights into whether and how CPPopt-based strategies might be beneficial, and (2) establishing support for the use of PbtO<sub>2</sub> as an adjunctive monitor for adequate or 'optimal' local perfusion.

**Methods:** We performed a retrospective analysis of a prospectively collected two-center dataset of patients with aSAH with or without later diagnosis of delayed cerebral ischemia (DCI). CPPopt was calculated as the CPP value corresponding to the lowest Pressure Reactivity index (PRx) (moving correlation coefficient of mean arterial and intracranial pressure). The relationship of (hourly) deltaCPP (CPP–CPPopt) and PbtO<sub>2</sub> was investigated using natural spline regression analysis. Data after DCI diagnosis were excluded. Brain tissue hypoxia was defined as PbtO<sub>2</sub> < 20 mmHg.

**Results:** 131 patients were included with a median of 44.0 [IQR 20.8–78.3] hourly CPPopt/PbtO<sub>2</sub> datapoints. The regression plot revealed a non-linear relationship between PbtO<sub>2</sub> and deltaCPP ( $p < 0.001$ ) with PbtO<sub>2</sub> decrease with deltaCPP < 0 mmHg and stable PbtO<sub>2</sub> with deltaCPP ≥ 0 mmHg, although there was substantial individual variation. Brain tissue hypoxia (34.6% of all measurements) was more frequent with negative deltaCPP. These dynamics were similar in patients with or without DCI.

**Conclusions:** We found a non-linear relationship between PbtO<sub>2</sub> and deviation of patients' CPP from CPPopt in aSAH patients in the pre-DCI period. CPP values below calculated CPPopt were associated with lower PbtO<sub>2</sub>. Nevertheless, the nature of PbtO<sub>2</sub> measurements is complex and the variability is high. Combined multimodality monitoring with CPP/CPPopt and PbtO<sub>2</sub> should be recommended as PbtO<sub>2</sub> probably gives adjunctive information about individual failure of homeostatic cerebral mechanisms.

P105

### Motor Evoked Potentials in Supratentorial Surgery as Diagnostic and Surrogate Biomarkers

E. Asimakidou, P. Alvarez Abut, A. Raabe and K. Seidel

Inselspital—Universitätsspital Bern, Switzerland

**Aim:** The objective of the current study was to assess the diagnostic and surrogate performance of MEPs in supratentorial surgery.

**Methods:** A Diagnostic Test Accuracy (DTA) analysis of MEPs for postoperative motor deficits and a correlation analysis between reversed intraoperative MEP changes and new postoperative motor deficits were performed. The data were visualized using the RevMan calculator in the Review Manager software (RevMan, version 5.4), MATLAB (version R2020b) and R (version 4.0.2, R-project.org).

**Results:** Sixty-eight studies were eligible for inclusion in these analyses. The DTA analysis revealed that MEPs have a high specificity and Negative Predictive Value (NPV) for early-transient, transient and permanent motor deficits. Sensitivity and Positive Predictive Value (PPV) estimates were inconsistent across the studies but were rather low or modest in the majority of them. Sensitivity yielded higher values for the threshold criterion compared with the amplitude criterion and PPV appeared to be higher when the mapping and monitoring criteria were combined compared with monitoring criteria alone. Diagnostic accuracy estimates were similar for Transcranial Electrical Stimulation (TES) and Direct Cortical Stimulation (DCS). The correlation analysis showed a negative correlation between the proportion of reversible MEP changes and the proportion of new postoperative motor deficits associated with MEP changes.

**Conclusions:** As diagnostic markers, MEPs exhibit high specificity and NPV and hence, the absence of irreversible MEP changes can reassure the surgeon both for short-term and long-term preservation of the motor function. However, MEPs display low to modest sensitivity and PPV, meaning that an irreversible MEP change is not associated per se with the occurrence of a postoperative motor deficit, although it is highly possible. As surrogate markers, MEPs perform well and successful reversal of a MEP alteration following a rescue intervention indicates an unimpaired motor function postoperatively.

## References

1. Macdonald, D.B. J. Clin. Neurophysiol. 2017; 34: 4–11.
2. Macdonald DB et al. Clin Neurophysiol. 2013;124(12):2291–316.
3. Holdefer, R.N. et al. Clin. Neurophysiol. 2016;127: 1717–1725.

P106

## Expanding the Indications for Measurement of Objective Functional Impairment in Spine Surgery: Diseases Affecting the Spinal Cord

G. Fischer <sup>1</sup>, V. Kälin <sup>1</sup>, O. P. Gautschi <sup>2</sup>, O. Bozinov <sup>1</sup> and M. Stienen <sup>1</sup>

<sup>1</sup> Cantonal Hospital St. Gallen, Switzerland

<sup>2</sup> Neuro- and Spine Center, Hirslanden Clinic St. Anna, Switzerland

**Aims:** Objective methods to quantify functional impairment are increasingly applied as outcome measures in patients with degenerative spine disease. However, these measures of objective functional impairment (OFI) are not validated for use in patients with spinal cord pathologies.

As spinal cord pathologies typically manifest with gait disturbances, we set out to quantify pre- and postoperative OFI in a standardized way.

**Methods:** In this pilot study we applied the Timed-Up-and-Go (TUG) test and/or the 6-min walking test (6WT) in four surgically treated patients with spinal cord dysfunction resulting from either extra- or intramedullary tumors, spinal cord herniation, arachnopathy or spinal cord tethering. OFI was determined by reporting age- and sex-adjusted OFI Z- or T-scores, based on normal population data. Outcome was determined before and after surgery and was related to the clinical condition of the patients. Change in function was evaluated based on minimum clinically important difference (MCID) values.

**Results:** Objective measured outcome correlated well with the subjective well-being of the patients at each time point. Two patients showed OFI preoperatively and in two patients a temporary decline in function was measured with subsequent recovery. At follow-up, three patients showed a clinically relevant improvement in function, improving by at least the MCID.

**Conclusions:** Standardized objective measurement of OFI was feasible in this pilot study. OFI as determined by either the TUG test or the 6WT resembled the functional status of the patient. We were able to quantify functional decline and/or improvement over time.

P107

### Factors Influencing Neurological Recovery after Surgical Treatment of Spinal Meningiomas in the Elderly: A Meta Analysis of Multiple Centers Experience

N. Tahhan <sup>1</sup>, A. Moiraghi <sup>2</sup>, A. Saladino <sup>3</sup>, V. Baro <sup>4</sup>, L. Paun <sup>5</sup>, F. DiMeco <sup>3</sup>, L. Denaro <sup>4</sup>, T. Meling <sup>6</sup>, E. Tessitore <sup>5</sup> and C. Barrey <sup>1</sup>

<sup>1</sup> Hospices Civils de Lyon, France

<sup>2</sup> Hôpitaux Universitaires de Genève, Switzerland

<sup>3</sup> Istituto Neurologico C. Besta, Italy

<sup>4</sup> University of Padova, Italy

<sup>5</sup> Hôpitaux Universitaires Genève, Switzerland

<sup>6</sup> Hôpitaux Universitaires de Genève, Switzerland

**Background:** Spinal meningiomas represent the most common spinal intradural tumors. MRI is the best diagnostic test, and surgical treatment results in excellent outcome.

**Methods:** We carried out an international multicentric retrospective analysis from the database of four referral hospitals. All the patients  $\geq 75$  years of age, diagnosed with spinal meningioma and treated surgically over a period of 20 years were included. Statistical tests using a univariate and multivariate ANOVA were achieved to find any outcome predictive factor(s). Approvement of the ethical comities from the 4 hospitals was obtained.

**Results:** 72 patients were included in the series which represent the largest series of spinal meningioma in the elderly in the literature until this day. The mean age of diagnosis was 80 year. The duration of symptoms was  $12 \pm 6.1$  months, with the most common location being the thoracic spine (87.3%). 62 patients (86.1%) presented postoperative improvement. The results observed in this study were comparable with the results reported in the literature from series with younger patients operated for spinal meningiomas making this surgery still indicated in the elderly.

**Conclusions:** The age and the severity of preoperative neurologic deficit did not lead to higher complication rate, but played a significant role in postoperative outcome.

P108

### Long-Term Outcome of Shunt Therapy in Patients with Idiopathic Normal Pressure Hydrocephalus

F. Kuser <sup>1</sup>, L. Stieglitz <sup>2</sup> and S. Fernandes Sargento Dias <sup>2</sup>

<sup>1</sup> University Zurich, Switzerland

<sup>2</sup> University Hospital Zurich, Switzerland

**Aims:** The syndrome of idiopathic normal pressure hydrocephalus (iNPH) is characterized by a slowly progressive clinical triad of gait disorder, cognitive decline and incontinence combined with ventricular dilation and normal mean intracranial cerebrospinal fluid (CSF) pressure. Studies on short-term outcome after shunt

implantation have shown a clinically significant improvement in 80% of patients after surgery. However, long-term results have rarely been published.

**Methods:** We aimed to evaluate the 6-year postsurgical follow-up of patients treated with a ventriculoperitoneal (VP) or ventriculoatrial (VA) shunt between 2012 und 2020 at the neurosurgical department of University Hospital Zurich. Preoperative patient selection was based on clinical evaluation, radiological findings, and CSF dynamic supplemental tests. Outcomes were assessed using the Kiefer Score and the NPH-Recovery Rate (NPH-RR). Secondly, the number of steps needed for 180° turn as a measure of gait disturbance, the Montreal Cognitive Assessment (MoCA) score as a measure of cognitive decline and continence of patients was recorded preoperatively and at last follow-up.

**Results:** 117 patients (aged  $74.3 \pm 8.0$  years) with mean preoperative DESH Score of  $6.8 \pm 2.8$  were included in this retrospective study. The mean preoperative Kiefer Score was  $7.4 \pm 3.1$ , significantly higher than the Kiefer Score 6 months, 1, 2, 3, 4 ( $p < 0.001$ ) and 5 years ( $p = 0.03$ ) after shunting. The lowest Kiefer Score of  $2.7 \pm 2.5$  was reached one year postoperatively with subsequent continuous slight increase to  $5.8 \pm 2.2$  at the 6-year postoperative follow-up. A satisfactory outcome according to the NPH-RR (NPH-RR  $\geq 2$ ) was observed in 74–86% of patients during the first 4 years postoperatively. The number of steps for 180° turn decreased from  $4.6 \pm 1.8$  preoperatively to  $3.1 \pm 1.1$  postoperatively. 23 of 117 patients (19.7%) underwent MoCA testing both pre- and postoperatively, with 8 patients (35%) showing significant improvement ( $\geq 3$  points). The proportion of incontinent patients decreased from 67.8% to 29.6%.

**Conclusions:** Patients with iNPH benefit significantly from shunt therapy up to 5 years postoperatively, with improvements noted among all components of the clinical triad.

P109

## Early Surgical Approaches in Pediatric Epilepsy—A Systematic Review and Meta-Analysis

N. Frank <sup>1</sup>, L. Greuter <sup>2</sup>, R. Guzman <sup>3</sup> and J. Soleman <sup>3</sup>

<sup>1</sup> Universitätsspital Basel und Universität Basel, Switzerland

<sup>2</sup> Univeristaetsspital Basel, Switzerland

<sup>3</sup> Universitätsspital Basel, Switzerland

**Introduction:** Pediatric seizures potentially have a severe negative impact on child's development. Therefore, successful control of epilepsy is the main aim in treating these patients. Drug-resistant epilepsy occurs in up to 30% of children suffering from seizures and about 10% qualify for surgical treatment. The aim of this systematic review and meta-analysis is to analyze the potential benefit of early epilepsy surgery in children concerning primarily seizure and developmental outcome.

**Methods:** PubMed and Embase databases were searched using a systematic search strategy to identify studies on pediatric epilepsy surgery under 3 years from their inception up to 2022. Outcome measures were seizure outcome, postoperative complications, seizure onset and reduction rate of antiepileptic drugs. A meta-analysis was thereafter performed for all included cohort studies. Risk of bias was assessed with Newcastle-Ottawa scale. Forest plots have been generated for all outcomes; risk ratio was used for pooled outcomes. A  $p$ -value of  $< 0.05$  was considered as significant.

**Results:** After removal of duplicates and after title screening, 70 articles were assessed for abstracts and 49 articles underwent full text evaluation. Finally, 12 articles were included. A total of 532 patients were analyzed with 401 patients (75%) receiving resective or disconnective surgery under the age of 3 years and 80 patients (15%) receiving surgery older than 3 years. The remaining 51 patients (9%) underwent VNS-implantation. Pooled outcome analysis for resective/disconnective surgery showed favorable outcome in 68% (95% CI [0.63, 0.73]), while comparative analysis between the age groups showed no



significant difference (77% early group and 75% late group; RR 1.03, 95% CI [0.73, 1.46]  $p = 0.75$ ). Favorable outcome for the VNS-cohort was seen in 52%, 65% in the early and 45.1% in the late group (RR 1.4393, 95% CI [0.87, 2.4]  $z = 1.42$ ,  $p = 0.16$ ). Developmental outcome was improved in 26%, 8.2% remained stable. Morbidity rate was moderate and showed no significant difference comparing the age groups, overall surgical mortality rate was very low (0.1%).

**Conclusions:** Epilepsy surgery in young pediatric age is a feasible and safe way to treat intractable epilepsy and therefore to potentially prevent severe developmental and cognitive deterioration. Further comparative studies of prospective nature, analyzing seizure but also developmental outcome, should be the focus of future studies.

P1110

### Impact of Very Small Aneurysm Size and Anterior Communicating Segment Location on Outcome after Aneurysmal Subarachnoid Hemorrhage

M. Roethlisberger <sup>1</sup>, S. Aghlmandi <sup>1</sup>, J. Rychen <sup>1</sup>, A. Chiappini <sup>1</sup>, D. W. Zumofen <sup>2</sup>, B. Schatlo <sup>3</sup>, M. Stienen <sup>4</sup>, C. Fung <sup>5</sup>, D. D'Alonzo <sup>6</sup>, N. Maldaner <sup>7</sup>, V. K. Steinsiepe <sup>4</sup>, M. V. Corniola <sup>8</sup>, J. Goldberg <sup>9</sup>, A. Cianfoni <sup>10</sup>, T. Robert <sup>10</sup>, R. Maduri <sup>11</sup>, G. Saliou <sup>12</sup>, D. Starnoni <sup>12</sup>, J. Weber <sup>4</sup>, M. A. Seule <sup>4</sup>, J. Gralla <sup>9</sup>, D. Bervini <sup>9</sup>, Z. Kulcsar <sup>13</sup>, J. Burkhardt <sup>14</sup>, O. Bozinov <sup>4</sup>, L. Remonda <sup>6</sup>, S. Marbacher <sup>6</sup>, K. Lövblad <sup>8</sup>, M. Psychogios <sup>1</sup>, H. C. Bucher <sup>1</sup>, L. Mariani <sup>1</sup>, P. Bijlenga <sup>8</sup>, K. A. Blackham <sup>1</sup> and R. Guzman <sup>1</sup>

<sup>1</sup> University Hospital of Basel, Switzerland

<sup>2</sup> Maimonides Medical Center, New York, USA

<sup>3</sup> University Hospital Göttingen, Germany

<sup>4</sup> Kantonsspital St. Gallen, Switzerland

<sup>5</sup> Medical Center, University of Freiburg, Switzerland

<sup>6</sup> Kantonsspital Aarau, Switzerland

<sup>7</sup> University Hospital Zürich, Switzerland

<sup>8</sup> Hôpitaux Universitaires de Genève, Switzerland

<sup>9</sup> Inselspital Bern, Switzerland

<sup>10</sup> Neurocenter of Southern Switzerland, Ospedale regionale, Switzerland

<sup>11</sup> Swiss Medical Network, Clinique de Genolier, Switzerland

<sup>12</sup> University Hospital Lausanne, Switzerland

<sup>13</sup> University Hospital Zurich, Switzerland

<sup>14</sup> Hospital of the University of Pennsylvania, USA

**Aims:** Very small anterior communicating artery aneurysms (vsACoA) of less than 5 mm in size are detected in a considerable number of patients with aneurysmal subarachnoid hemorrhage (aSAH). Single-center studies report that vsACoA harbor particular risks when treated. This nationwide multicentric study, based on an unselected cohort derived from the Swiss Subarachnoid Hemorrhage Outcome Study (SwissSOS), assesses the radiological outcome(s) after aneurysm treatment and clinical outcome(s) at discharge of aSAH-patients diagnosed with vsACoA and compares outcomes to results observed for aneurysms in other locations.

**Methods:** Information on 1868 patients was collected in the SwissSOS-registry between 2009–2014. The primary outcomes were presence of a new stroke on computed tomography (CT) after aneurysm treatment and presence of a new focal neurological deficit (FND) at discharge. Secondary outcomes were in-hospital rebleeding, functional status (modified Rankin-scale) and overall mortality rates.

**Results:** The study analyzed 1258 aSAH patients with a male prevalence of 34%, 439 of which had a documented ruptured ACoA with a male prevalence of 48%. Patients harboring a vsACoA (prevalence 12%,  $n = 144$ ) presented with a higher median Body-Mass-Index when compared to patients with larger ACoA-aneurysms. Very-small aneurysm size and ACoA location was not associated with the occurrence of a peri-interventional stroke or a neurological deficit, correlated negatively with a higher

modified Rankin-scale (aOR 0.65, 95% CI 0.49–0.85) at discharge and correlated positively with death at 1-year (aHR, 1.65, 95% CI 1.01–2.71).

**Conclusions:** Constitutional and treatment-related factors may explain a worse prognosis of aSAH patients with very small ruptured aneurysms in the long-term.

P111

### High Precision Bone Cutting by Er: YAG Lasers Might Minimize the Invasiveness of Navigated Brain Biopsies

T. T. Ha <sup>1</sup>, F. M. Thieringer <sup>2</sup>, M. Bammerlin <sup>3</sup> and D. Cordier <sup>4</sup>

<sup>1</sup> University Hospital of Basel, Switzerland

<sup>2</sup> University and University Hospital Basel, Switzerland

<sup>3</sup> Advanced Osteotomy Tools AG, Switzerland

<sup>4</sup> University Hospital Basel, Switzerland

Biopsies of brain tissue are sampled and examined to establish a diagnosis and to plan further treatment, e.g., for brain tumors. The neurosurgical procedure of sampling brain tissue for histologic examination is still a relatively invasive procedure that carries several disadvantages. The question of this “proof of concept”-study is to answer the question if laser technology might be a potential tool to make brain biopsies less invasive, faster and safer. Laser technology might potentially enable us to miniaturize the burr hole and also to angulate the burr hole much more tangential in relation to the bone surface in order to take biopsies from brain regions that are usually only difficult to access. We examined if it is possible to miniaturize the hole in the skull bone to such a high extent that potentially the laser-created canal itself may guide the biopsy needle with sufficient accuracy. The 2-dimensional, i.e., radial tolerance of the tip of biopsy needles inserted in these canals was measured under defined lateral loads which mimic mechanical forces applied by a surgeon. The canals through the skull bones were planned in angles of 90° (perpendicular) and 45° relative to the bone surface. We created a total of 33 holes with an Er: YAG laser in human skull bones. We could demonstrate that the achievable radial tolerance concerning the guidance of a biopsy needle by a laser created bone canal is within the range of the actual accuracy of a usual navigated device if the canal is at least 4 mm in length. Lateral mechanical loads applied to the biopsy needle had only minor impact on the measurable radial tolerance. The latter opens the perspective to sample biopsies in brain areas that are usually not or only hazardous to access.

P112

### Major Trauma in Children—Take a Close Look at the Craniocervical Junction

A. Bürgin <sup>1</sup>, B. Willi <sup>1</sup>, C. Zweifel <sup>2</sup> and S. Stricker <sup>2</sup>

<sup>1</sup> Pädiatrie, Kantonsspital Graubünden, Switzerland

<sup>2</sup> Neurochirurgie, Kantonsspital Graubünden und Universitätsspital Basel, Switzerland

**Introduction:** In children traumatic spine injuries are typically located in the uppercervical segment. Diagnosis of potentially fatal occipitocervical distraction injuries is important and can be challenging. We report a case of a boy with an atlantooccipital dislocation after a high velocity accident who presented with bilateral abducens nerve palsy.

**Case report:** A 11-year-old boy was admitted to the emergency room after a high velocity sledding accident while wearing a helmet. At admission he had oral bleeding, was hemodynamically stable and had a normal neurological exam. The initial CT showed mandibular fractures, a fracture of the femur and a retroclival hematoma. The patient underwent surgical stabilization of the femur fracture. Secondary clinical survey revealed

a complete abducens nerve palsy on the left, and an incomplete palsy on the right. MRI showed, in addition to the retroclival hematoma, a dislocation of the tectorial membrane from the clivus and an anterior atlantooccipital ligament injury with consequent partial atlantooccipital dislocation. He was treated with a soft collar for neck immobilization and alternate patching of the eyes to prevent diplopia. At 4 month follow-up the abducens palsy completely recovered on both sides, leaving the boy without any neurological sequelae.

**Discussion:** Occipitocervical distraction injuries are more often seen in children due to relatively smaller occipital condyles, a more horizontally orientated atlantooccipital articulation and generally greater ligamentous laxity. Diagnosis can be challenging because of wide clinical presentation and difficult detection on CT. The abducens nerve is especially vulnerable to trauma due to its anatomic course. In occipitocervical distraction injuries it can be compressed by an associated retroclival hematoma, damaged by accompanying petrous bone fractures as well as shearing and contusion of the nerve or brainstem. Although most of these palsies (73%) show spontaneous recovery after six months, bilateral and complete palsy are predictors of a poorer outcome.

**Conclusions:** In patients with severe trauma and abnormalities on initial CT or presence of neurological deficits cerebral MRI is important. To look for occipitocervical distraction injuries the craniocervical junction should be included on MR-imaging. Abducens nerve palsy can be a warning sign for these occipitocervical distraction injuries, and usually recovers within 6 months.

P113

### Morphometric Evaluation of Meckel's Cave and its Impact on Trigeminal Rhizotomy

M. Oertel, G. Iliukhina, L. Stieglitz

University Hospital Zurich and University of Zurich, Switzerland

**Aims:** Ganglion Gasseri rhizotomy is a well-known and established option in the treatment of trigeminal pain (TP). The extent to which the morphology and size of Meckel's cave (MC) potentially influence the procedure and its success is largely unknown. For this reason, the authors systematically evaluated the configuration and dimensions of MC.

**Methods:** In 31 TP patients undergoing trigeminal rhizotomy, high resolution 3 Tesla magnetic resonance imaging-based three-dimensional quantitative volumetric analyses were performed for a morphometric study of Meckel's cave. In addition, patient data and surgical outcome were systematically evaluated. Finally, the morphometric data and clinical results were compared.

**Results:** While most patients had an oval shape of MC (19/31) and more frequently (11/31 vs. 8/31) improved in pain postoperatively, 9/31 patients had a triangular MC shape and predominant reduction of TP (7/31 vs. 2/31) and 3/31 patients had a round shape of MC with improvement of TP in 2/31 vs. 1/31 cases. The volume of the MC ranged between 0.15 and 0.55 cm<sup>3</sup> (mean 0.34 cm<sup>3</sup>). Most patients benefited clinically following surgery (20/31), 8/31 showed no improvement while 3/31 patients even worsened. No significant correlation between clinical outcome and volume of MC was found.

**Conclusions:** Whereas influences of the study design and of various clinical or interventional factors on the results cannot be excluded, we did not find a clear association between MC volumes and clinical outcome. However, our data suggests that predominantly a triangular shape of MC containing the trigeminal ganglion could contribute to improve postoperative results of TP patients.

P114

### ZAP-X® Gyroscopical Radiosurgery—Introduction of the Technology and First Preliminary Results

C. Weber <sup>1</sup>, C. Picardi <sup>1</sup>, K. Klucznik <sup>2</sup>, E. Taub <sup>3</sup>, D. Weltz <sup>1</sup>, B. Dettinger <sup>1</sup>, R. Guzman <sup>3</sup>, L. Mariani <sup>3</sup> and A. Mack <sup>1</sup>

<sup>1</sup> SNRC—Swiss Neuro Radiosurgery Center, Switzerland

<sup>2</sup> Radiotherapie Hirslanden, Switzerland

<sup>3</sup> Universität Basel, Universitätsspital Basel, Switzerland

**Introduction:** ZAP-X is a dedicated high-precision cranial radiosurgery irradiator that uses a self-shielded gyroscopically suspended linac instead of Co 60 sources. Beam geometry and beam quality are similar to the Gamma Knife (SAD 45 cm, 3 MV) and the tracking algorithms are from the CyberKnife. The linac moves within two hemispheres, whose axes are tilted at a 45° angle to each other and radiate onto the intrinsic unit center point, through which the target is moved on a 3-axis table [1].

**Methods:** 5 plans each calculated on different platforms (CyberKnife, Varian Edge and ZAP-X) for 4 indications (vestibular schwannoma, meningioma, pituitary adenoma and trigeminal neuralgia) were compared with regard to coverage, Paddick Conformity Index, Gradient Index, load of the respective risk structures (OARs) and the out-of-field dose. In addition to the Winston-Lutz test, a complex system test (end-to-end test) was also carried out.

**Results:** The planning comparison of the different device types resulted in an average coverage of 98.18 (SD 0.15) for the CyberKnife, 98.26 (SD 0.13) for the Varian Edge and 98.46 (SD 0.11) for the ZAP-X. The mean conformity was 1.34 (SD 0.19) for the CyberKnife, 1.38 (SD 0.21) for the Varian Edge and 1.29 (SD 0.16) for the ZAP-X. With the ZAP-X, a somewhat steeper dose gradient could be achieved in almost all plans (GI approx. 3). The isocenter stability, averaged over a time interval of 6 months, was 0.39 mm (SD 0.1) for the CyberKnife, 0.37 mm (SD 0.1) for the Varian Edge and 0.32 mm for the ZAP-X (SD 0.1) and were therefore almost identical for all device classes.

**Conclusions:** The planning comparison shows that a very steep dose gradient can be achieved with the ZAP-X due to the beam guidance, the short distance (SAD) and the small penumbra, and the out-of-field dose can thus be reduced. Clinical results are expected to be comparable to those of the Gamma Knife®.

P115

### Topographic Distribution of Inflammation Factors in a Healing Aneurysm

B. Grüter <sup>1</sup>, G. Boillat <sup>1</sup>, J. Hägler <sup>1</sup>, R. Jeannine <sup>1</sup>, S. Wanderer <sup>1</sup>, M. von Gunten <sup>2</sup>, J. Galvan <sup>3</sup>, R. Grobholz <sup>1</sup>, H. Widmer <sup>3</sup>, L. Remonda <sup>1</sup>, L. Anderegg <sup>1</sup> and S. Marbacher <sup>1</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> Institute of Pathology Laenggasse, Switzerland

<sup>3</sup> Universität Bern, Switzerland

**Background:** Aneurysm healing after endovascular treatment relies on biological processes such as neointima formation and organization of the early intraluminal hematoma into mature scar tissue. Thereby, activation and deactivation of the inflammation cascade plays an important regulatory role. We hypothesize, that in addition to the timely evolution, also the topographic distribution of inflammation factors is of paramount importance for successful aneurysm healing.

**Methods:** Decellularized saccular sidewall aneurysms were microsurgically created in Whistar rats. They were treated by coiling and compared to the natural course of

untreated aneurysms after 3 days ( $n = 16$ ), 7 days ( $n = 19$ ) and 21 days ( $n = 8$ ). Upon follow-up, aneurysms were harvested, macroscopically inspected and light microscopically assessed for healing and inflammation status. Furthermore, immune histology was performed to visualize inflammation cells (CD45, CD3, CD20, CD31, CD163, HLA-DR, tryptase clone AA) and an in-situ hybridization was performed for soluble inflammation markers (IL 6, MMP2, MMP9, TNF- $\alpha$ , FGF23, VEGF). These factors were assessed in four regions of interest (ROIs): aneurysm wall (proximal and distal), neointima, intraluminal (in the thrombus) and in the adjacent vessel wall.

**Results:** Coiled aneurysms showed an enhanced pattern of thrombus organization and neointima formation, whereas those without coils demonstrated a heterogeneous pattern of thrombosis, thrombus recanalization, and aneurysm growth ( $p = 0.02$ ). Whereas pro-inflammatory cytokines were ubiquitously detected in all four ROIs, inflammation cells tended to accumulate inside the thrombus, and to a lesser extend in the neointima ( $p = 0.001$ ). Inside the evolving thrombus, there was a concentration of B-lymphocytes, M1-macrophages and mast cells ( $p < 0.0001$ ), whereas endothelial cells accumulated directly in the neointima ( $p < 0.0001$ ). Their presence is associated with complete aneurysm healing.

**Conclusions:** The presence of proinflammatory cells plays a crucial role in aneurysm remodelling after coiling: Whereas thrombus organization is hallmarked by a pronounced intra-thrombotic inflammation reaction, neointima formation is characterised by direct invasion of endothelial cells, which promote complete aneurysm healing. The presented topographic distribution of regenerative inflammatory processes may pave the way for future treatment modalities that enhance aneurysm healing after endovascular therapy.

P116

## Evaluation of Biomechanical Properties of Various Alloplastic Implant Materials for the Replacement of Bony Defects of the Skull

S. Busch <sup>1</sup>, N. Sharma <sup>2</sup>, D. Cordier <sup>1</sup> and F. M. Thieringer <sup>2</sup>

<sup>1</sup> Department of Neurosurgery, University Hospital Basel, Basel, Switzerland

<sup>2</sup> Clinic of Oral and Cranio-Maxillofacial Surgery, University Hospital Basel, Basel, Switzerland

**Background:** Defects of the bony skull are usually treated by replantation of the previously removed bone segment. However, the replantation of autologous bone material carries several specific risks: increased incidence of infections, resorption and others. As an alternative patient-specific implants (PSI) were used, which are preoperatively manufactured based on imaging data. Materials employed for this purpose are bone cement (e.g., polymer methyl methacrylate (PMMA)), plastics (e.g., polyetheretherketone (PEEK)), metals (e.g., titanium), or ceramics. The objective of the study was to compare human skull bone with different implant materials regarding specific biomechanical properties.

**Material and Methods:** Ten fresh-frozen human skull bones were precisely cut to an identical geometry by an Erbium: YAG-Laser (CARLO®, Cold Ablation Robot-guided Laser Osteotomes, AOT, Basel, Switzerland). Cranial PSIs with an identical geometry as the standard calotte were fabricated in medical and implantable-grade materials such as PMMA, milled & 3D printed PEEK. The fabricated PSIs ( $n = 30$ ) were digitized using an optical scanner for assessment of geometric accuracy. In addition, the biomechanical properties of the PSIs and bone samples were assessed in a quasi-static mechanical test setup.

**Results:** We report preliminary data of testing. The lowest force until fracture for the bone samples ( $n = 10$ ) was 1227.8 N with 6 mm displacement, the highest force was 3527.9 N with 13 mm displacement. This huge difference is due to variable bone thickness. The PMMA samples ( $n = 10$ ) broke at a force of 1485.6 N with 4.6 mm displacement values.

The milled PEEK PSI (n = 10) didn't break and withstood a force of 2427.5 N at 24 mm displacement, after which the tests were stopped. The 3D printed PEEK samples (n = 10) broke at a force of 1302.5 N with 8 mm displacement. Preliminary data of the accuracy assessment showed a root mean square error (RMSE) of 0.78 mm for PMMA, 0.40 mm for milled PEEK and 0.49 mm for 3D printed PEEK.

**Conclusions:** Our preliminary data showed a difference in fracture force and displacement depending on the manufacturing technology (3D printed vs. milled) which should be considered in future models. Accuracy assessment showed the lowest RMSE for milled PEEK and the highest for PMMA but all under 1 mm which is clinically acceptable.

P117

### Combined Approaches with Planned Subtotal Resection and Radio-Neurosurgery for Large Skull-Base Meningiomas: A Retrospective Single Center Experience

C. Tuleasca <sup>1</sup>, D. Starnoni <sup>2</sup>, R. T. Daniel <sup>2</sup> and M. Levivier <sup>2</sup>

<sup>1</sup> CHUV Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland

<sup>2</sup> Lausanne University Hospital (CHUV), Switzerland

**Introduction:** Meningiomas are the most common primary intracranial tumor. Microsurgical resection is the core treatment for large meningiomas with symptomatic mass effect.

**Methods:** Here, we present our experience with combined approaches (surgery and radio-neurosurgery on the residual tumor) in Lausanne for large meningiomas, particularly those located at the level of skull-base, over a period of 12 years (2010–2022). Mean patient's age at surgery was 57.2 months (median 55, 39–83.7). The anatomical location was: petroclival (n = 8, with various extensions), petrous face (n = 5), cavernous sinus (n = 2), jugular foramen, torcular, petrotentorial, spheno-orbital and parasagittal, each with one case. The residual part was located at the level of the upper clivus (n = 6, with further residue extending on the Meckel's cave and/or cavernous sinus), jugular foramen (n = 5), cavernous sinus (n = 5), internal acoustic canal and brainstem/middle clivus (n = 2), torcular and transverse sinus (n = 1), superior sagittal sinus (n = 1).

**Results:** Mean follow-up period after Gamma Knife (GK) radio-neurosurgery was 47.2 months (median 48, 3–108). Mean preoperative tumor volume was 21.4 mL (median 16.4, 2.3–69.3), at time of GK was 6.2 mL (median 5.1, 1.7–16.3) and at last follow-up was 4.8 mL (median 2.7, 1.2–14.1). Sixteen patients underwent one microsurgical resection, while 3 underwent 2 and one went 3. Immediate surgical complications included ischemic stroke at the level of the pons (n = 1), partial thrombosis of right transvers and sigmoid sinus clinically silent (n = 1), ischemic stroke and further cerebellar oedema (n = 1), medulla oblongata stroke (n = 1). Radiosurgery was performed after a mean interval of 6.5 months (median 5.2, 2.4–17.4). All patients had been treated in single fraction GK (12–14 Gy marginal dose) except one which underwent hypofractionated GK. Five patients had volume-staged single fraction treatments. At last follow-up, the late clinical assessment showed no deficit in 8 cases. One patient had complete visual recovery, while two had partial visual recovery. Complications after GK included a peritumoral cyst enlargement at 12 months after radiosurgery, which needed a fenestration within the fourth ventricle.

**Conclusions:** The management of large meningiomas, particularly at the level of skull-base is challenging. Combined approaches with planned subtotal resection followed by GK can help in functional preservation, while attaining high levels of tumor co.

P118

### Gait Analysis in Home Environment for Assessment of VP-Shunt Responsiveness in iNPH Patients

S. Fernandes Dias <sup>1</sup>, C. Graf <sup>2</sup>, E. Jehli <sup>3</sup>, M. F. Oertel <sup>3</sup>, J. Mahler <sup>3</sup>, M. Schmid Daners <sup>2</sup> and L. H. Stieglitz <sup>3</sup>

<sup>1</sup> University Hospital Zurich and University of Zurich, Switzerland

<sup>2</sup> Product Development Group Zurich, ETH Zurich, Switzerland

<sup>3</sup> University Hospital of Zurich, University of Zurich, Switzerland

**Aims:** Through the use of movement gait sensors we aimed to characterize the gait pattern in iNPH patients in the home environment by the differentiation from healthy elderly controls (EHC).

**Methods:** Five wearable inertial measurement units were placed for 72 h in eleven iNPH patients and 20 age and sex matched EHCs. Data was collected in home environment. Fifteen spatio-temporal gait parameters were analysed. iNPH patients were examined preoperatively and within 6 months of postoperative follow-up. In the iNPH group a sub-analysis was performed to assess differences between responders (NPH- recovery rate  $\geq 5$ ) versus non-responders. We further aimed to identify parameters able to predict a reliable response to VP-shunt placement.

**Results:** There was a significant difference for most of gait parameters between EHC and iNPH patients. Postoperatively, iNPH patients showed an improvement of the swing phase ( $p = 0.039$ ). Patients with a good response to VP-shunt placement (NPH RR  $\geq 5$ ) showed a significant improvement on the parameters gait velocity, stance to swing ratio, stance phase, cycle time and cadence.

**Conclusions:** A significant difference on the analysed gait parameters was observed between EHC and iNPH patients. The only parameters that did not significantly varied were the foot outward rotation and swing phase. iNPH patients showed an improvement of gait after VP-shunt placement, with this being more evident in the NPH-responders-cohort.

P119

### The Use of Chiasmopexy for the Treatment of Skull Base Meningioma

S. Diaz <sup>1</sup>, D. Starnoni <sup>2</sup>, C. Tuleasca <sup>2</sup>, M. Levivier <sup>2</sup> and R. Daniel <sup>2</sup>

<sup>1</sup> CHUV Lausanne, Switzerland

<sup>2</sup> CHUV, Lausanne, Switzerland

**Aim:** The proximity to the optic apparatus (OA) and the risk of radiation-induced optic neuropathy often prevents many surgeons from proposing complementary stereotactic radiosurgery (SRS) for residual parasellar meningiomas involving the cavernous sinus or it can limit the therapeutic prescribed dose. Placement of a fat graft between the optic nerve (ON) and the tumor (chiasmopexy or neuropexy) may allow to maintain the distance gained at surgery and to deliver the optimal dose.

We aim to evaluate the radiological temporal profile and evolution of the radiological signal of the fat graft following chiasmopexy and its implication in planning post-operative SRS.

**Methods:** A single-center, retrospective consecutive cohort study of patients in whom the chiasmopexy technique was used following resection of a meningioma located at the parasellar region.

MRIs were analyzed to determine the tumor characteristics, extent of resection and the exact volume of the fat graft. The autograft signal ratio was evaluated on all sequences based on the signal of the pons.

Distance between residual tumor and OA and therapeutic delivered doses were measured and compared with a hypothetical treatment plan that could have been possible immediately after surgery (based on immediate post-operative MRI).

**Results:** 23 patients were included (Clinoid meningioma (57%), sphenoid-orbital meningioma (30%), tuberculum sellae meningioma (13%)). Upfront radiosurgery was performed in 14 out of 17 patients with residual tumor (82.3%). 8 patients had hypofractionated dose Gamma-knife due to the close proximity to the OA.

The fat graft showed a progressive significant loss of volume within 12 months ( $p$ -value = 0.034), with 37% of residual volume at 12-month follow-up. Volume reduction was correlated to the decrease in signal ratio in T2 and T1 sequences ( $r = 0.8$ ) and to the increase in gadolinium-injected T1 sequences ( $r = -0.8$ ).

The hypothetical treatment plan showed that a single dose treatment would have been possible for the entire patient cohort thanks to chiasmopexy. No patients experienced a post radiosurgical worsening deficit nor recurrence, with a mean follow-up of 65.57 months (range, 28–128 months).

**Conclusions:** Chiasmopexy allows to maintain distance between residual tumor and OA gained at surgery and to deliver the optimal SRS dose while keeping the dose received by the optic nerve below 8 Gy. Early treatment with SRS, within 3 months post-op, could be the optimal time point.

P120

### Robustness of the Wide-Field Imaging Muller Polarimetry for Brain White Matter Fiber Tract Identification in Surgery-like Environment—An Ex Vivo Study

L. Felger <sup>1</sup>, E. Hewer <sup>2</sup>, T. Maragkou <sup>3</sup>, R. McKinley <sup>4</sup>, M. Murek <sup>1</sup>, T. Novikova <sup>5</sup>, A. Pierangelo <sup>5</sup>, O. Rodríguez-Núñez <sup>1</sup>, I. Zubak <sup>1</sup> and P. Schucht <sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Inselspital, Bern University Hospital, University of Bern, 3010, Bern, Switzerland

<sup>2</sup> Lausanne University Hospital and University of Lausanne, 1011 Lausanne, Switzerland

<sup>3</sup> Institute of Pathology, University of Bern, 3010, Bern, Switzerland

<sup>4</sup> Support Center for Advanced Neuroimaging (SCAN), University Institute of Diagnostic and Interventional Radiology, University of Bern, Inselspital, Bern University Hospital, 3010, Switzerland

<sup>5</sup> LPICM, CNRS, Ecole polytechnique, IP Paris, Palaiseau, 91128, France

**Aims:** A real-time, non-invasive, dye- and contact-free brain tissue differentiation during tumor neurosurgery is a challenge we address with the wide-field imaging Mueller polarimetry (IMP) [1,2]. In our prior studies we demonstrated that IMP is capable to detect correctly the in-plane orientation of brain white matter fiber tracts of a flat formalin-fixed thick brain specimen. Here we demonstrate the versatility and robustness of IMP data for the detection of cerebral white matter fiber tracts in the adverse conditions similar to those present in neurosurgery, such as uneven surfaces and presence of blood and irrigation fluids.

**Methods:** We used the non-contact wide-field IMP system [3] operating in a visible wavelength range in reflection configuration for surface imaging in 3 settings using fresh cadaveric calf brain. First, we performed MP images of coronal sections and repeated the images after removing a thin layer of white matter using a cavitron ultrasonic surgical aspirator (CUSA) comparing their respective polarimetric characteristics. Next we mimicked lesion resection by performing 3 cm-deep resection cavities with i) a scalpel and ii) a CUSA commonly used in neurosurgery in order to compare the corresponding polarimetric maps. Lastly, we performed tests with dilution series of blood spilled on prepared white matter specimen and measured the Mueller matrix images acquired at 550 nm and 650 nm, processed with Lu-Chipman decomposition algorithm [4].

**Results:** For uneven surfaces due to ultrasonic aspiration and within resection cavities made with scalpel and CUSA, the measurements performed with IMP system maintained



their respective sensitivity. The orientation of the white matter fiber tracts was clearly visualized in the image of the azimuth of the optical axis. At the same time, the presence of blood/saline solution up to a thickness of 2 mm did not significantly impact the orientation maps.

**Conclusions:** Our wide-field IMP system produces robust results on fiber tract visualization under all adverse, neurosurgery-like conditions, rendering it a potential new tool for an intra-operative, real-time, non-invasive identification of brain tumor borders and brain fiber tract orientation.

P121

### Effects of Two Types of Exercise Training on Psychological Well-Being, Sleep, Quality of Life and Physical Fitness in Patients with High-Grade Glioma (WHO III and IV)

A. Saemann <sup>1</sup>, L. Eisenhut <sup>2</sup>, L. Staub <sup>2</sup>, S. Brand <sup>2</sup> and D. Cordier <sup>1</sup>

<sup>1</sup> Universitätsspital Basel, Switzerland

<sup>2</sup> University of Basel, Switzerland

**Background:** Although there is evidence concerning physical activity (PA) and its effect on quality of life (QoL) in cancer patients, there is so far no conclusive evidence concerning PA in patients with high-grade glioma (WHO grade III and IV). Given this, endurance and strength training were employed to investigate their impact on symptoms of depression, feelings of stress and anxiety, fatigue, insomnia, and physical fitness, compared to an active control condition. Up to now, many studies with the aim to analyze those interconnections failed due to poor patient recruitment, very extensive study design, exhaustive and numerous training sessions, or high dropout rates. Thus, the main aim of this pilot study is to examine the feasibility of the created innovative study protocol and to assess potential tendencies.

**Methods:** Designed for a total of 45 patients, we included up to this interim analysis 29 patients (mean age 52.07, SD = 12.45, 55.2% women), who were randomly assigned to either endurance training, strength training or to an active control condition (i.e., psychological counseling), before starting adjuvant therapy after tumor surgery. The intervention took place for 6 consecutive weeks, consisting of 2 weekly sessions for all groups. Measurements took place at baseline, three and six weeks after onset of adjuvant therapy, with the last measurement representing the end of study. For all psychological dimensions we used standardized questionnaires at all three measurement-points. Aerobic capacity was assessed by the 6-min walking test and measurement of handgrip strength served as surrogate marker for upper body strength.

**Results:** The protocol was shown to be feasible with high recruitment rates (90%), low dropout rates (13%) and good adherence. Taking the limited number of study participants in this pilot study into account, the pattern of results suggests that endurance training and the active control condition may improve dimensions of depression, stress and anxiety. Further, exercise interventions seem not to change physical fitness, but potentially to increase fatigue.

**Conclusions:** As a consequence of the proven feasibility of the study protocol, this protocol will serve as the basis for an upcoming large scale multicenter trial. Our data suggest tendencies that endurance training and psychological counseling may have favorable impact on psychological well-being among patients with HGG after tumor resection and undergoing radiochemotherapy.

P122

### Immunotherapeutic Targeting of Fibroblast Activation Protein (FAP) using CAR-T Cells in Treatment Refractory Glioblastoma

N. Tatari <sup>1</sup>, T. Schenker <sup>1</sup>, R. Ritschard <sup>1</sup>, A. Zingg <sup>1</sup>, H. Thut <sup>1</sup>, M. Etter <sup>1</sup>, N. Rodrigues Mantuano <sup>1</sup>, L. Jeker <sup>1</sup>, F. Stenner <sup>1</sup>, U. Petrasch <sup>2</sup>, C. Renner <sup>2</sup>, H. Läubli <sup>1</sup> and G. Hutter <sup>1</sup>

<sup>1</sup> University Hospital Basel and University of Basel, Department of Biomedicine, Basel, Switzerland

<sup>2</sup> Hirslanden Clinic Zurich, Switzerland

**Introduction:** Glioblastoma (GBM) is the most common malignant primary adult brain tumor, characterized by extensive cellular and genetic heterogeneity 1. The Standard of Care (SOC) therapy and clinical trials have not been successful in improving patients' survival which underscores an urgent need for developing new effective therapies for this treatment refractory disease 2,3.

**Aim:** In vitro and in silico analysis revealed high level of Fibroblast Activation Protein (FAP) expression in GBM tissue but not on normal brain tissue making FAP a safe therapeutic target 4. As Chimeric antigen receptor (CAR) expressing T cells have shown promising results against multiple cancers in the past few years, we hypothesized that targeting FAP by CAR-T cells would be a promising approach for the treatment of GBM.

**Methods:** To investigate this hypothesis, we assessed the efficacy of FAP CAR-T cells against GBM preclinically at in vitro and in vivo level using patient derived GBM samples as well as patient derived xenograft mouse model of GBM, respectively.

**Results:** Our data revealed that co-culturing CAR-T cells with GBM organoids resulted in increased surface expression of T-cell activation markers. Moreover, activated T cells showed higher release of pro-inflammatory cytokines including TNF- $\alpha$  and IFN- $\gamma$ . FAP CAR-T mediated cytotoxicity against GBM organoids was also observed in the co-culture of CAR-T cells and GBM cells. Treatment of GBM tumor-bearing mice with FAP CAR-T yielded extended survival in mice and significant reductions in tumor burden.

**Conclusions:** These rigorously obtained data suggest that clinical development of this therapeutic modality can provide a novel therapeutic strategy for GBM patients which can be used in combination with other immunotherapeutics.

P123

### How Much Space Is Needed for Decompressive Surgery in Malignant Middle Cerebral Artery Infarction: Enabling Single Stage Surgery

M. Montalbetti <sup>1</sup>, S. Lörcher <sup>1</sup>, A. Nowacki <sup>1</sup>, L. Häni <sup>1</sup>, W. J. Z'Graggen <sup>2</sup>, A. Raabe <sup>1</sup> and P. Schucht <sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland

<sup>2</sup> Department of Neurology and Department of Neurosurgery, Inselspital, Bern University Hospital and University of Bern, Switzerland

**Background:** Decompressive hemicraniectomy (DCE) is routinely performed for ICP control after malignant middle cerebral artery (MCA) infarction. Despite the undisputed life-saving benefit of DCE, trephined patients are at risk of traumatic brain injury and the syndrome of the trephined until cranioplasty. Additionally Cranioplasty (CP) after DCE is itself associated with high complication rates.

Single stage surgical strategies with overlaying brain protection by an autologous or artificial bone flap may eliminate the aforementioned problems.

**Objective:** Assess the additional volume needed for safe expansion of the injured brain to enable single stage decompressive surgery.

**Methods:** We performed a retrospective radiological and volumetric analysis of all patients that had DCE in our clinic between January 2009 and December 2018 and had

appropriate pre- and postoperative imaging. We investigated prognostic parameters in perioperative imaging and checked clinical outcome.

**Results:** Of 86 patients with DCE, 44 fulfilled the inclusion criteria. The median diameter of the bone flap was 157.2 mm (95% CI 153.5 mm–163.0 mm). Median brain swelling was 75.35 mL (95% CI 69.42 mL–97.02 mL). Median bone flap volume was 113.3 mL (95% CI 104.3 mL–121.6 mL). The median brain swelling above the outer skull rim was –1.62 mm (95% CI –2.33 to –0.54 mm). Only one (2.2%) patient had a shearing injury at the craniotomy border.

Patients whose brain swelled more than the volume of removed Bone (n = 9) either had multiple territories involved (n = 3), had a dissection of the internal carotid artery (ICA) (n = 4), thrombus location at the carotid T (n = 5), preexisting ICH (n = 1), failed thrombectomy (n = 1) or a combination of those. No patient had a simple M1 occlusion.

**Conclusions:** In 79.6% of the patients studied, the volume of removed bone alone was equivalent to or larger than the additional intracranial volume needed for brain swelling. In the remaining 20.4% the required volume was only marginally larger. A decompressive surgical strategy allowing for both safe brain expansion and single stage surgery should be possible as long as the surgeon strives for as larger decompression than 12 cm. Patients with simple M1 occlusion seem to be ideally suited for this.

P124

### Twiddler's Syndrome after Dorsal Root Ganglion Stimulator Implantation: A Case Report and Review of the Literature

A. L. Schütz, R. Mija and J. Schlaeppli

Inselspital, Switzerland

**Objectives:** Twiddler's syndrome is a rare hardware complication of implantable pulse generators (IPG), associated with repeated coiling and twisting of the IPG and leads. This has been described in cardiac pacemakers and deep brain stimulators although recently it has been documented in patients with spinal cord stimulators. To our knowledge, we report the first case of a patient with dorsal root ganglion stimulation developing Twiddler's syndrome and review the current literature.

**Materials and methods:** A 51-year old woman with complex regional pain syndrome of the foot and calf after malleolar fracture received dorsal root ganglion stimulation of the left L5 and S1 nerve roots. The IPG was implanted abdominally on the right. The patient showed pain reduction from NRS 9 to 5. Over the following four months, the patient reported severe pain along the pocket, connector and extension leading to the IPG. Fluoroscopy showed lead entanglement with strain of the electrodes. Revision surgery was planned.

Intraoperatively, the extension leads were completely entwined and twisted, resulting in extensive strain on the connector and IPG. The DRG-electrodes were damaged and the distal contacts of the leads torn out. The electrodes were replaced and the IPG implanted lumbar on the right. After surgery the patient described complete resolution of her pain.

**Results:** Twiddlers syndrome has been described in up to 7% of patients with cardiac pacemakers, 1.5% with DBS and 0.5% with SCS. Despite growing reports in the literature, the pathophysiology remains unclear. Deliberate or subconscious manipulation of the device as well as the result of muscle contraction on the IPG are possible mechanisms. Old age, female gender, obesity, abdominal site of implantation and psychological disorders may be risk factors for development of this syndrome.

Our patient was female, obese and had initially her IPG implanted abdominally, all of these being described as risk factors for developing Twiddlers syndrome.

**Conclusions:** To our knowledge, we report the first case of Twiddlers syndrome with implantable pulse generators for dorsal root ganglion Stimulation. As in spinal cord

stimulation, the awareness of this syndrome may prevent its occurrence. Especially in obese patients, IPG-placement in the lumbar region should be considered.

P125

### Neuroinflammation after Subarachnoid Hemorrhage: Is Losartan the Panacea of Choice the Medical Community Waited for?

S. Wanderer <sup>1</sup>, J. Konczalla <sup>2</sup>, J. Mrosek <sup>2</sup>, S. Kashefiolasi <sup>2</sup>, C. Musahl <sup>1</sup>, S. Marbacher <sup>1</sup>, G. A. Schubert <sup>1</sup> and L. Andereggen <sup>1</sup>

<sup>1</sup> Kantonsspital Aarau, Aarau 5000, Switzerland

<sup>2</sup> Goethe-University Hospital, Schleusenweg 2–16, 60528 Frankfurt am Main, Germany

**Background:** Poor patients' outcome after aneurysmal subarachnoid hemorrhage (SAH) is owed a multifactorial process. Delayed cerebral vasospasm (DCVS), ischemic neurological deficits and infarction are the most feared acute sequelae triggered by enhanced synthesis of serotonin (5-HT) and endothelin-1 (ET-1). During the past decades, multiple drugs have been analyzed for protective effects without resounding success. Therefore, authors wanted to analyze a potential beneficial role of Losartan (LOS). **Methods:** Male Sprague Dawley rats were either randomized to an injection of blood in the cisterna magna (SAH group) twice or to isotonic sodium chloride (sham group). Animals were culled on Day 5 and basilar artery ring segments used for in vitro tension studies.

**Results:** LOS, applied in a concentration of 10–3 M was able to significantly reduce 5-HT ( $p < 0.01$ ) and ET-1 ( $p < 0.05$ ,  $p < 0.01$ ) mediated vasoconstriction in sham segments.

**Conclusions:** These findings, beside its well known beneficial effects on restoring the impaired endothelin-B1-receptor function after SAH as well on the neuroprotective and antiepileptogenic aspect, might be implemented in pushing forward tailored concepts to sufficiently ameliorate patients' functional outcome after SAH.

P126

### Dosimetric Plan Comparison between the Novel ZAP-X Radiosurgery Device and the CyberKnife System for Vestibular Schwannomas

C. Weber <sup>1</sup>, C. Picardi <sup>1</sup>, B. Dettinger <sup>1</sup>, D. Weltz <sup>1</sup>, A. Mack <sup>1</sup> and K. Klucznik <sup>2</sup>

<sup>1</sup> SNRC—Swiss Neuro Radiosurgery Center, Switzerland

<sup>2</sup> Radiotherapie Hirslanden, Switzerland

**Introduction:** Stereotactic radiosurgery is a well established treatment modality for vestibular schwannomas (VS). Its excellent local control rate and the low toxicity profile were proven by several clinical trials. Nevertheless, an increased risk of hearing loss was reported for single fraction SRS for patients receiving more than 4 Gy to the cochlea. Especially in the case of intrameatal lesions located close to the inner ear, achieving the proposed constraints for the cochlea might be challenging. ZAP-X is a novel radiosurgery device using 3 MV X-rays for the treatment of intracranial lesions. Although the ZAP-X is becoming increasingly popular in radiosurgery, robust dosimetric comparative data with other established dedicated radiosurgery devices is still lacking. In our study we aim to perform a dosimetric plan comparison between CyberKnife (CK) and the ZAP-X for 5 VS and report on the differences concerning the most important plan parameters.

**Material and methods:** Five intrameatal VS of Koos grade 1 and 2 within a volume range between 0.06 cc and 1.21 cc were chosen for the dosimetric comparison. The treatment planning was carried out independently by trained medical physicists on the CK System and on the ZAP-X, and was based on the same structure sets including the PTV and the OARs.

Since the conventional chosen prescription isodose varies significantly between the two devices (typically 70–80% for CK and 40–60% for ZAP-X) planners were free to choose the prescription isodose, which ensured optimal target coverage with the given prescribed dose while respecting the OARs constraints. For the comparison of the plans the target-specific parameters (Coverage, New Conformity Index (nCI), gradient index (GI)) and the doses received by the OARs were evaluated.

**Results:** The most significant difference between ZAP-X (average 3.33) and CK (average 5.51) showed up in the GI. The nCI varied between 1.17 and 1.53 for ZAP-X and 1.07 and 1.55 for CK. An excellent coverage above 99% for all cases was achieved by both modalities. The cochlea maximum dose was significantly better for ZAP-X (average 3.2 Gy) than for CK (average 6.3 Gy), as well as the cochlea mean dose (1.63 Gy vs. 3 Gy).

**Conclusions:** The novel ZAP-X radiosurgery device convinces with a high conformity and steep dose fall off, which is at least comparable to the plan parameters published for the CK. In terms of sparing the OAR, the ZAP-X plans delivered better results compared to CK.

P127

### Critical Review of Classification Systems of Craniopharyngiomas

N. Tahhan, V. Delabar, T. Jacquesson, A. Vasiljevic, G. Raverot, R. Manet and E. Jouanneau

Hospices Civils de Lyon, France

**Introduction:** Craniopharyngiomas are rare tumors whose delicate management requires a multidisciplinary approach. Several clinico-radiological classification systems have been proposed, making it possible to determine the optimal management, in particular the surgical approach that seems most appropriate. In this study, we present a critical review of the literature concerning the most used classification systems and propose a synthetic classification.

**Methods:** A critical review of the literature was conducted, querying the Medline database, with the following keywords: ((craniopharyngioma) AND (classifications)).

**Results:** The Kassam classification (Kassam et al. 2008) is a surgical classification that divides craniopharyngiomas according to their relationship to the pituitary stalk. Although the classification is useful in deciding the surgical approach, it does not mention tumors of the pituitary stalk. The mammillary body angle (MBA) (Pascual et al. 2013) is a radiological measurement on MRI which is used to study the relationship between the tumor and the third ventricle (intraventricular or extraventricular). Unfortunately, this angle can only predict this relationship at 83%, which can pose an intraoperative problem in the event of misinterpretation. The Prieto classification (Prieto et al. 2017) is one of the most widely used classifications. It takes into consideration multiple radiological criteria depending on the tumor relationship with the third ventricle (tumor displacement of the third ventricle, angle MBA optic chiasm, pituitary stalk, signal from the hypothalamus, shape of the tumor, supposed origin of the tumor). Unfortunately, in this classification we also find no mention of tumors of the pituitary stalk, the use of different MRI sequences to determine adherence to the hypothalamus or the importance of mammillary tubercles. The ideal classification must describe the position vis-à-vis the infundibulo-tuberal tract (chiasm, MBA), the position of the mammillary tubercles which must be preserved and the peri-tumoral hypothalamic signal which is heterogeneous indicating an invasion limiting the surgical possibilities.

**Conclusions:** Clinico-radiological classifications have brought an advance in the therapeutic planning of craniopharyngiomas. However, they remain incomplete and not totally reliable. A synthetic classification is proposed to calculate the approach and tumor resectability.

P128

### Personality Alterations Following Resection of Large Anterior Sagittal Sinus Meningioma Evidenced by Self-Other Voice Discrimination Task: A Case Report

P. Orepic <sup>1</sup>, G. R. Iannotti <sup>2</sup>, C. Goga <sup>2</sup>, H. Julien <sup>2</sup>, S. Betka <sup>1</sup>, H. Park <sup>3</sup>, O. Blanke <sup>1</sup>, C. M. Michel <sup>2</sup>, G. Bondolfi <sup>2</sup> and K. Schaller <sup>2</sup>

<sup>1</sup> École polytechnique fédérale de Lausanne EPFL, Switzerland

<sup>2</sup> University of Geneva, Switzerland

<sup>3</sup> Taipei Medical University, Taiwan

Personality alterations following neurosurgical procedures pose a major concern for patients and remain poorly understood both by clinicians and neuroscientists. Hence, there is a strong need for documented reports involving post-surgical personality changes, in order to gain sufficient knowledge potentially leading towards established clinical protocols for risk assessment of alterations in patients' sense of self following surgery (1). Here, we report a case of a 51-year-old female patient who underwent bi-frontoparietal craniotomy for the resection of a large sagittal sinus meningioma with bilateral extension, including resection and ligation of the superior sagittal sinus. The resection was followed by personality alterations and a group of behavioral phenomena that mimic certain characteristics of the Gastaut-Geschwind syndrome—such as hypergraphia, hyperspirituality with some delusional traits, a deepened cognitive and emotional responses and hyposexuality—although a temporal epilepsy has never been objectified. These clinical observations were further reflected and experimentally quantified with a series of behavioral and neuroimaging tasks assessing self-other voice discrimination, an established marker for self-consciousness (2). In all tasks, the patient consistently confused self- and other voices—i.e., she misattributed other-voice stimuli to herself and self-voice stimuli to others. Moreover, behavioral findings were corroborated with scalp EEG results. Specifically, the same EEG microstate, that was in healthy participants associated to hearing own voice (3), in this patient occurred more often for other-voice stimuli, that the patient misattributed to herself. We hypothesize personality alterations might be accounted by the development of a large venous collateral haemodynamic network that followed gradual occlusion and subsequent resection of the sagittal sinus, thereby impacting blood supply of brain areas associated to self-consciousness. We discuss this case report in the light of neural mechanisms underlying the sense of self and the relevance for developing experimental biomarkers of post-surgical personality alterations.

P129

### A Rare Case of Meningioma of Foramen of Monro: Case Report and Technical Note

K. Papadimitriou, F. Marrone, A. Simonin, K. Al-Taha, J. Fournier

Hopital du Valais (HVS)—Centre Hospitalier du Valais Romand, Switzerland

**Introduction:** Meningiomas are usually benign, solid tumors that account for approximately 13–40% of the intracranial neoplasms, making them the second most common intracranial tumor in adults with an incidence of 1.5–5.5 per 100,000. Intraventricular meningiomas (IVMs) are rare of which the majority located in the lateral ventricles. However, foramen of Monro meningioma (FOM) is an uncommon site of origin. Endoscopic techniques have been mainly utilized for skull base meningiomas. We report the first case of a fully endoscopic removal of a FOM.

**Case report and technical note:** A 66-year-old female presented to our department with lower limbs paresthesias for 3 weeks, progressively involving the upper limbs, and gait instability. A brain magnetic resonance imaging (MRI) revealed a 14 mm intraventricular

mass localized on right foramen of Monro, provoking obstructive hydrocephalus. The tumor was iso-intense on T1 and T2-weighted images. Following gadolinium administration, a homogeneous enhancement was observed. The patient underwent an endoscopic resection via a right frontal burr-hole under neuronavigation guidance. Histopathological analysis revealed an OMS grade 1 meningioma. The postoperative course was uneventful, with complete symptoms resolution. Immediate post-operative CT scan revealed resolution of hydrocephalus. Follow-up MRI at 6 months confirmed complete resection and resolution of hydrocephalus.

**Discussion:** IVM frequently occur in the trigone of the lateral ventricle. According to the literature, their distribution is 58.6% in the lateral ventricle, 34.5% in the third ventricle and 6.9% in the fourth ventricle. Foramen of Monro meningiomas are extremely rare and sparsely reported in the literature. To the best of our knowledge a total of 6 cases of FOM have been reported. They were resected with microsurgical techniques, namely the interhemispheric transcallosal approach. Our case represents the first fully endoscopic removal of FOM. In our experience, the endoscopic technique is safe and offers good surgical and clinical outcomes in carefully selected cases. Factors that influence the ability of a surgeon to perform a complete endoscopic resection include tumor size, composition, vascularity and surgeon's experience.

*P130*

### **Single Burr Hole Endoscopic Evacuation of Contralateral Interdural Hematoma following Resection of a Tuberculum Sellae Meningioma: A Case Report**

**D. Kiss-Bodolay, K. Papadimitriou, J. Fournier**

Hopital du Valais (HVS)—Centre Hospitalier du Valais Romand, Switzerland

**Introduction:** Inter-dural hematoma (IDH) are encapsulated between the layers of the convexity dura mater. Until nowadays, 11 cases have been reported in the literature. Here we report the first case of an endoscopic evacuation of a left IDH that developed following the resection of a tuberculum sellae meningioma via a right subfrontal approach.

**Case report:** A 60-year-old woman operated in our department for a tuberculum sellae meningioma via a right fronto-basal craniotomy with a Simpson grade II resection. On the 3-month follow-up, the head magnetic resonance imaging (MRI), revealed a newly formed contralateral left convexity hematoma. The collection was localized over the left convexity and was crossing the sutures like a subdural hematoma. It was however biconvex like an epidural hematoma. Although the patient was asymptomatic, because of the size of the collection, the midline shift and its epidural localization we decided to evacuate the collection in the most minimally invasive fashion. With the aid of neuro-navigation a single burr hole centered on the outer convexity of the hematoma is performed. Following piercing the outer membrane resulted in the outflow of a liquid that had a typical chronic blood aspect often described as “motor oil”. An opaque dura like thick yellowish hemorrhagic membrane is observed under with irregular darker yellowish spots smoothly in continuity with all of its walls like a proper dural pocket. A small piece of the inner membrane is sharply dissected and sent for histopathological identification which confirmed its dural origin. The patient remained neurologically intact and was discharged on postoperative day 3. The six month follow up MRI showed complete resolution of the hematoma with no residual collection.

**Discussion:** The pathophysiology of the IDH is unknown. IDH is likely an underdiagnosed entity because of its rare incidence and unknown radiological features. In fact, the radiological characteristics of the IDH could be described as uniquely chimeric. Endoscopic burr hole evacuation of subdural hematoma in our experience is a safe procedure and it is associated with good clinical outcomes. IDH should be kept in the

differential diagnosis in case of biconvex convexity collections that is crossing the sutures. However, this is a single center case report and therefore further prospective multicenter studies should be contacted.

P131

### The Frontal Aslant Tract and Its Possible Role in Language: Report of Four Patients after Low Grade Glioma Surgery

A. Consuegra <sup>1</sup>, K. Seidel <sup>1</sup>, W. Corina <sup>2</sup>, S. Sandra <sup>2</sup>, P. Alvarez Abut <sup>1</sup>, A. Raabe <sup>1</sup> and P. Schucht <sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland

<sup>2</sup> Department of Neurology and Neurorehabilitation, Speech therapy section, Inselspital, Bern University Hospital, Switzerland

**Introduction:** The frontal aslant tract (FAT) and its role in language has been widely discussed in patients presenting primary progressive aphasia (PPA) and more importantly in patients undergoing glioma surgery. Based on the current literature, this tract may play a role in speech initiation and fluency. However, controversy between surgical centers exists regarding the necessity to identify and to preserve the FAT during glioma resection.

**Methods:** We report four patients undergoing surgery for a low-grade glioma of the left frontal lobe and visual disconnection of the FAT in the postoperative tractography. Two patients were right-handed and two left-handed. One right-handed patient was operated asleep. The remaining three patients underwent awake surgery with intraoperative speech mapping. MRI with DTI sequences were performed both preoperative and postoperative. Fibertracking of the FAT was analyzed using the iPlan FiberTracking software (Brainlab, Munich). Tracking parameters included a FA of 0.15, a minimum length of 50 mm and a maximal angulation of 45°. Postoperative reports of physicians and speech therapists were analyzed for language deficits.

**Results:** The final histopathology revealed an oligodendroglioma WHO CNS grade 2 in two patients and an astrocytoma WHO CNS grade 2 in the remaining two patients. Three of the patients presented postoperative moderate (one patient) to mild (two patients) language deficits, mainly consisting in fluency and self-initiated speech disorders, which were described in the speech therapist reports. These deficits improved but persisted on a lower extend 2 to 3 months after surgery, even though neurological rehabilitation was completed. Longer follow ups are missing. No language deficits were described in the speech therapists reports of one left-handed patient. However, the neuropsychological reports one month after surgery described a lower performance in terms of verbal fluency as well as a subjective difficulty in terms of word finding.

**Conclusions:** Our data support the already described role of the FAT in speech fluency. Fluency and self-initiated speech deficits seem to persist at least in the short to mid postoperative term, however, to a moderate to mild extent. This highlights an oncological challenge regarding quality of life during resection of low-grade gliomas in the left frontal lobe. Larger cohorts of patients with longer follow-ups are needed to understand whether patients recover completely.



P132

### The Sylvian Keyhole Craniotomy for Microsurgical Clipping of Middle Cerebral Artery Bifurcation Aneurysms: A Technical Nuance to the Minipterional Craniotomy

A. Saemann, J. Rychen, M. Röthlisberger, J. Soleman, G. Hutter, L. Mariani, R. Guzman

Universitätsspital Basel, Switzerland

**Background/Objective:** In the past decade, the continuing quest for minimally invasive microsurgical approaches has resulted in the minipterional craniotomy. Despite these improvements, a degree of painful postoperative mastication and temporomandibular joint dysfunction remains postoperatively. The Sylvian keyhole craniotomy offers an advanced variation of the minipterional craniotomy for the treatment of middle cerebral artery (MCA) aneurysms. It doesn't aim to reach the skull base and is centered over the MCA bifurcation aneurysm. The aim of this study is to compare the minipterional and Sylvian keyhole craniotomy for the microsurgical clipping of MCA bifurcation aneurysms regarding operative accessibility and surgical maneuverability.

**Methods:** This study is a descriptive comparative anatomical study performed on two injected cadavers' heads with concomitant VR reconstruction of their CTA imaging. Surgical accessibility of the MCA bifurcation, the ability to gain direct proximal control and release of CSF in the carotid cistern was assessed. The study was conducted with the adjunct of virtual reality and 3D printed models.

**Results:** The sylvian Keyhole approach provides a direct trajectory towards the bifurcation of the second segment (M2) of the MCA and beyond, while providing proximal control (M1), allowing CSF release, and offering a good working corridor for clipping of MCA aneurysms. It offers a safe and feasible variant for microsurgical treatment of MCA-aneurysms. There is no need for drilling of the bony sphenoid wing ; associated risks, morbidity, and time expenditure are reduced. The consequence is an enhanced cosmesis due to a smaller incision and less invasive manipulation.

**Conclusions:** The sylvian keyhole craniotomy might be a promising pathology-tailored, minimally invasive approach for microsurgical clipping of MCA-aneurysms distal to the limen insulae. The proof of concept should be evaluated in the setting of a clinical study.

P133

### Patient and Caregiver Reported Outcome Measures after Single-Level Selective Dorsal Rhizotomy in Pediatric Patients with Spastic Cerebral Palsy

A. Rasadurai <sup>1</sup>, N. Frank <sup>2</sup>, L. Greuter <sup>2</sup>, M. Licci <sup>3</sup>, P. Weber <sup>4</sup>, S. Jünemann <sup>4</sup>, R. Guzman <sup>3</sup> and J. Soleman <sup>3</sup>

<sup>1</sup> Faculty of Medicine, University of Basel, Basel, Switzerland. Department of Health Sciences and Technology, ETH Zürich, Zurich, Switzerland. Department of Pediatric Neurosurgery, University Children's Hospital of Basel (UKBB), Basel, Switzerland

<sup>2</sup> Department of Pediatric Neurosurgery, University Children's Hospital of Basel (UKBB), Basel, Switzerland

<sup>3</sup> Faculty of Medicine, University of Basel, Basel, Switzerland. Department of Pediatric Neurosurgery, University Children's Hospital of Basel (UKBB), Basel, Switzerland

<sup>4</sup> Department of Neuropediatrics, University Children's Hospital of Basel (UKBB), Basel, Switzerland

**Aims:** The aim of this cohort study is to assess the outcome of single-level selective dorsal rhizotomy (SDR) in children with spastic cerebral palsy (CP) treated at our institution, focusing on patient-reported outcome measures (PROMs) and quality of life (QoL) of patients and their caregivers.

**Methods:** We included consecutive patients undergoing SDR from 2018 to 2020 at our institution. Subjective outcome was measured through PROMs, while functional outcome

was measured through baseline characteristics, operative outcome, as well as short- and long-term follow-up. Furthermore, the effect of age at the time of surgery on patient/caregiver satisfaction was analyzed.

**Results:** Seven children (3 female, 43%) with a median age at surgery of 11.9 years (IQR 8.7–15.5) were included. All patients had a GMFCS score of at least IV before surgery. Five surgeries were palliative and two non-palliative. Based on PROMs, SDR showed very good QoL, and health-related outcome measures for both palliative and non-palliative patients. Patients/caregivers satisfaction was higher for the early subgroup (age  $\leq 11$ ) than the late subgroup (age  $> 11$ ). Functional outcome showed reduced spasticity in both groups. Blood transfusions were never needed, while no CSF leak, infection, or permanent morbidity was seen.

**Conclusions:** Based on PROMs of our cohort, SDR leads to high satisfaction and improved QoL, especially if done at an early age. Further studies with larger cohorts are necessary to underline and confirm our observations.

P134

### Risk Factors for Postoperative Cerebrospinal Fluid Leakage after Intradural Spine Surgery

C. M. Jesse, H. Schermann, J. Goldberg, M. Gallus, L. Häni, A. Raabe and R. T. Schär

Inselspital, Universitätsspital Bern, Switzerland

**Aims:** Well-defined risk factors for cerebrospinal fluid leakage (CSFL) following intradural spine surgery are scarce in the literature. The aim of this study was to identify patient and surgery related risk factors and the incidence of CSFL.

**Methods:** For this retrospective cohort study, we identified consecutive patients who underwent intradural spine surgery between 2009 and 2021 at our department. Primary endpoint was the incidence of clinically or radiologically proven CSFL. The impact of clinical and surgical factors on occurrence of CSFL was analyzed.

**Results:** In total, 375 patients (60.3% female, mean age  $54 \pm 16.5$  years) were included. Thirty patients (8%) had postoperative CSFL and thereby a significantly higher risk for wound healing disorders (OR 24.9, CI 9.3–66.7) and surgical site infections (SSIs; OR 8.4, CI 2.6–27.7) ( $p < 0.01$  for each).

No patient-related factors were associated with CSFL. Previous surgery at the index level correlated significantly with postoperative CSFL (OR 2.76, CI 1.1–6.8,  $p = 0.03$ ) in multivariate analysis. Furthermore, patients with intradural tumors tended to have a higher risk for CSFL (OR 2.3, CI 0.9–5.8,  $p = 0.07$ ). Surgery related factors did not influence occurrence of CSFL. Surgery on the thoracic spine had a significantly lower postoperative CSFL rate than surgery on the cervical or lumbar spine (OR –2.5, CI 1.3–4.9,  $p = 0.02$ ).

**Conclusions:** Our study found no modifiable risk factors for preventing CSFL after intradural spine surgery. Patients with previous surgery at the index level were at higher risk for CSFL. CSFL resulted in significantly more wound healing disorders and SSIs necessitating further therapy.

P135

**Prediction of MRI in Intra-Operative Findings for Spinal Arachnoid Diseases****N. Tahhan, G. Capo, F. Cotton, I. Zaed and C. Barrey**

Hospices Civils de Lyon, France

**Background:** A large variety of spinal arachnoid diseases are described in the literature, and differential diagnosis is often complex, requiring a good knowledge of the different entities and accurate neuroimaging.

**Objective:** The purpose of this article was to depict through a clinical series of surgical cases the most relevant diagnostic features of these pathologies on the commonly utilized MRI sequences (T1, T2-weighted), and to correlate them with intraoperative findings.

**Material and methods:** Five patients are presented and extensively discussed, one for each spinal arachnoid disease: spinal arachnoid web, arachnoiditis, idiopathic spinal cord herniation, intradural arachnoid cyst, extradural arachnoid cyst. All the cases were surgically treated in the same institution (BLINDED). We underline imaging clues and intraoperative findings for differential diagnosis, to help physicians to elaborate the right management before going to the operating room.

**Results:** All cases were successively operated with resolution of preoperative symptoms. Six key-radiological features were selected, helping differential diagnosis: localization (intra/extradural/both), aspect of the spinal cord (compressive effect/displacement/scalpel sign), arachnoid bride, CSF turbulent flow, vertebral scalloping, and absence of contrast enhancement.

**Conclusions:** MRI demonstrated excellent correlation with intra-operative findings and permitted, when carefully analyzed, to prepare adequately the surgical procedure. Although rare, these spinal arachnoid diseases must be recognized by clinicians considering that appropriate treatment most often permit to relieve the symptoms.

P136

**Giant Mastoid Emissary Vein and Retrosigmoid Approach: Case Report and Review of the Literature****L. Weman, K. Papadimitriou, J. Fournier and A. Simonin**

Hôpital de Sion, CHVR, Switzerland

**Abstract**

**Background and Importance:** Mastoid emissary vein is a highly variable anatomical structure to be wary of in neurosurgery especially in planning a retrosigmoid approach. Here, we report an unusual case of a giant mastoid emissary vein in a patient undergoing microvascular decompression for trigeminal neuralgia. Radiological and intraoperative pictures are presented, as well as a literature review.

**Case report:** A 54 years-old patient presented with a V1-V2 left trigeminal neuralgia for 10 years. Magnetic resonance imaging (MRI) did not show clear evidence of neurovascular conflict with the trigeminal nerve. Because of conservative management failure, a microvascular decompression with nerve combing was performed. During surgical planning, an exceedingly large, prominent left mastoid emissary vein draining into the sigmoid sinus was identified. Internal opening measured 7 mm of diameter and external opening measured 13 mm.

**Results:** Careful approach and early recognition of the large mastoid emissary vein was performed, to avoid excessive bleeding. The postoperative course was uneventful, with a marked decrease in symptoms, and without any new neurological deficit. Immediate post-operative CT scan did not show any complication.

**Conclusions:** To the best of our knowledge, this is the first report of a giant mastoid emissary vein during a retrosigmoid approach. Pre-operative imaging and surgical planning should be done cautiously to avoid excessive bleeding or sinus thrombosis.

P137

### Evaluation of the Placement of Ventricular Derivations Using an Adapted Frameless Navigation System Compared to the Freehand Technique for Narrow Ventricles

J. Haemmerli, P. Constanthin, D. Kiss Bodolay, L. Paun, G. Patet, A. Lavé, K. Schaller and P. Bijlenga

Hôpitaux Universitaires de Genève, Switzerland

**Aims:** External ventricular derivation (EVD) is a potentially life-saving procedure, which neurosurgical residents are supposed to become acquainted with early in their cursus. EVD may cause morbidity/mortality if not well placed, i.e., in case of narrow ventricles following traumatic brain injury. This study aims to evaluate the accuracy of EVD placement using an adapted frameless navigation system compared to the standard freehand procedure for narrow ventricles.

**Methods:** Twenty-eight consecutive EVD inserted in the operating room were retrospectively analyzed in patients with an Evan's index under 0.35. For navigated EVD, the VarioGuide (Brainlab®) system was used. A navigated biopsy needle was inserted in the EVD, substituting the stylet. Navigated EVDs were placed according to a pre-planned trajectory. Navigated and freehand techniques were compared. Primary outcome was the distance between the tip of the EVD and the foramen of Monro. Secondary outcome were the Kakarla score, the number of punctures, EVD-related bleeding rate and the surgical time.

**Results:** N = 11 navigated and N = 17 freehand EVDs were performed. No difference was observed regarding the Evan's index between groups ( $p = 0.06$ ). The median tip-to-Monro distance was significantly shorter in the navigation-group compared to the freehand-group (respectively: median 0 mm (IRQ:2.6); median 9.25 mm (IRQ:15.0),  $p < 0.001$ ). EVD placement scored as Kakarla 1 in 100% in the navigation-group and 47,1% in the freehand-group ( $p = 0.02$ ). Rate of first hit were 100% in the navigation-group and 82.4% in the freehand-group ( $p < 0.001$ ). Six EVD-related bleedings were observed in the freehand-group (35.3%) and one in the navigated-group 9.1% ( $p = 0.02$ ). Surgical time did not differ between groups ( $p = 0.46$ ).

**Conclusions:** In case of narrow ventricles, the use of the adapted frameless navigation system for EVD placement shows a higher accuracy with a reduced number of punctures compared to the freehand technique. Neurosurgical residents should be aware of this technique.

P138

### Retrosigmoid Approach for Neurovascular Decompression of Glossopharyngeal Nerve for a Glossopharyngeal Neuralgia

K. Al-Taha, K. Papadimitriou, A. Simonin and J. Fournier

Hopital du Valais (HVS)—Centre Hospitalier du Valais Romand, Switzerland

**Introduction:** Glossopharyngeal neuralgia emerging from a neurovascular conflict at the root exit zone of the glossopharyngeal nerve is a rare pain syndrome characterized by a brief episodic unilateral stabbing pain with abrupt onset and cessation, in the in the sensory distribution of the ninth cranial nerve. Surgery for glossopharyngeal neuralgia is challenging due to the complex anatomy and irregular shape of the jugular foramen, and

its intimate neurovascular relationships such as the carotid artery anteriorly, the facial nerve antero-laterally, the hypoglossal nerve medially and the vertebral artery inferiorly. Here we report the case of a 46 year old female suffering from glossopharyngeal neuralgia due to conflict of left PICA (posterior inferior cerebellar artery).

**Methods:** Patient is positioned in a prone position with the ipsilateral shoulder supported on a 30° gel rest. The head is immobilized on a 3-point head-clamp, rotated 30° towards the ipsilateral shoulder and flexed 20° towards the floor. The genu of the sigmoid sinus is placed at the highest point of a perpendicular line that bisects the sinodural angle. Reverse Trendelenburg position is applied to the surgical bed to facilitate venous return. A standard left retrosigmoid approach was performed. The spinal nerve of XI nerve was followed to the jugular foramen. By utilizing neuromonitoring the glossopharyngeal nerve was identified. A small piece of Teflon was placed between the left glossopharyngeal nerve and PICA. Under direct vision of neuro-endoscope no other vascular conflict was identified.

**Conclusions:** The retrosigmoid approach to the jugular foramen offers good surgical exposure and outcomes in carefully selected patients suffering from glossopharyngeal neuralgia due to vascular conflict. Precise understanding of the relationship between osseous anatomy of the jugular foramen, dural architecture dividing the jugular foramen, neural location and trajectory, vascular venous and arterial structures and muscular anatomy is imperative.

\*The authors contributed equally to this work.

P139

### Anterior Lumbar Interbody Fusion in Elderly Patients: Peri- and Postoperative Complications and Clinical Outcome

C. M. Jesse <sup>1</sup>, L. Mayer <sup>1</sup>, L. Häni <sup>1</sup>, J. Goldberg <sup>1</sup>, A. Raabe <sup>1</sup>, O. Schwarzenbach <sup>2</sup> and R. T. Schär <sup>1</sup>

<sup>1</sup> Inselspital, Universitätsspital Bern, Switzerland

<sup>2</sup> dasRückenzentrum AG, Switzerland

**Aims:** Anterior lumbar interbody fusion (ALIF) is an effective surgical technique for treating various lumbar pathologies but its use in elderly patients is controversial. Data concerning complications and effectiveness are sparse. We investigated peri- and postoperative complications, radiographic parameters and clinical outcome in elderly patients.

**Methods:** Patients  $\geq 65$  years who underwent ALIF between January 2008 and August 2020 were included. All surgeries were performed through a retroperitoneal approach. Clinical and surgical data as well as radiological parameters were collected prospectively and analyzed retrospectively.

**Results:** A total of 39 patients were included, mean age 72.6 ( $\pm 6.3$ ) years (range 65–90 years); mean American Society of Anesthesiologists (ASA) risk classification was 2.3 ( $\pm 0.6$ ). A laceration of the left common iliac vein was the only major complication recorded (2.6%). Minor complications occurred in 20.5% of patients. Fusion rate was 90.9%. Reoperation rate at index level was 12.8% and 7.7% in adjacent segments.

The multidimensional Core Outcome Measures Index (COMI) improved from 7.4 ( $\pm 1.4$ ) to 3.9 ( $\pm 2.7$ ) after 1 and to 3.3 ( $\pm 2.6$ ) after 2 years. Oswestry disability index (ODI) improved from 41.2 ( $\pm 13.7$ ) to 20.9 ( $\pm 14.9$ ) and 21.5 ( $\pm 18.8$ ) after 1 and 2 years, respectively. Improvements of at least the minimal clinically important change score of 2.2 and 12.9 points in the ODI and COMI after 2 years were noted in 75% and 56.3% of the patients, respectively.

**Conclusions:** With careful patient selection ALIF is safe and effective in elderly patients.

P140

**Spontaneous Thrombosis of a Vein of Galen Malformation in the Adults: Case-Report****N. Tahhan<sup>1</sup>, A. T. Khalid<sup>2</sup>, C. Dumot<sup>1</sup>, R. Riva<sup>1</sup> and I. Pelissou-Guyotat<sup>1</sup>**<sup>1</sup> Hospices Civils de Lyon, France<sup>2</sup> Centre Hospitalier Universitaire Vaudois, Switzerland

The vein of Galen malformation (VGAM) are usually found in childhood and rarely described in the adult. There are two major types of presentation: hemodynamic failure in neonates due to massive shunt, and venous hypertension during infancy. VGAM are treated by endovascular methods in the majority of cases.

We present a rare case of a 40 years old patient with incidental finding of VGAM who presented a spontaneous thrombosis and a complete restoration of the deep venous system followed by a review of the literature of resembling cases.

P141

**Microsurgical Dissection of a Dorsal Arachnoid Web with D-Wave Intra-Operative Neuromonitoring: Technical Note****G. Zegarek, J. Fournier and A. Simonin**

Hôpital du Valais—Centre Hospitalier du Valais Romand (CHVR), Switzerland

**Abstract****Aims:** Background and Importance

Spinal Arachnoid Web (SAW) is an exceedingly rare condition that can present with focal neurological deficits with or without syrinx formation. Although hallmark radiological and clinical features are well described in the literature, standard neurosurgical treatment is still being discussed for this rare entity. We describe 2 cases of dorsal SAW operated by microsurgical resection under intra-operative neuromonitoring (IONM) by D-wave at a single neurosurgical center.

**Methods:** Case Report

Both patients were 42-year-old males who presented with early signs of dorsal myelopathy. The spinal pre-operative MRIs showed signs compatible with SAW, notably the typical “scalpel sign” for both patients. One SAW was at the D4-D5 level with an associated syringomyelia, while the other was at the D7-D8 level without associated syrinx. Both patients underwent dorsal laminoplasty with microsurgical resection of the SAW under D-wave IONM.

**Results:** The postoperative clinical course was favourable for both patients with improved neurological exam. Postoperative MRI showed the disappearance of the posterior imprint on the thoracic spinal cord after SAW resection. The advent of D-wave technology has proven effective and reliable, and is considered by many to be mandatory for intramedullary spinal cord tumors. We believe it could be expanded to focal spinal arachnopathies.

**Conclusions:** Our experience applying D-wave neuromonitoring to SAW surgery demonstrated its effectiveness and safety. We believe that this form of IONM could be applied to focal spinal arachnopathy surgery.

P143

# Brain Injury Burden Based on MRI Assessment of Regional Cerebral Blood Flow (rCBF) in Former Professional Football Players

E. Danielli <sup>1</sup>, S. Ulmer <sup>2</sup>, N. Simard <sup>1</sup> and M. Noseworthy <sup>1</sup><sup>1</sup> McMaster University, Canada<sup>2</sup> neurorad.ch, Switzerland

**Aims:** Due to the countless sub-concussive and concussive blows to the head, high contact sport can lead to cumulative neurological damage and possible dementia in athletes [1]. The aim of this study was to use regional cerebral blood flow (rCBF) measured with MRI arterial spin labelling (ASL) and a personalized Z-scoring approach to quantify focal brain damage and left/right symmetry in individual retired Canadian Football League (CFL) players. We aimed to determine if rCBF or spatial coefficient of variance (sCoV) were abnormal in retired athletes relative to healthy controls. It was hypothesized that former athletes would exhibit bilateral abnormalities in brain regions-of-interest (ROIs).

**Methods:** Data from 17 retired Canadian Football League (CFL) players (male, aged  $58 \pm 6.32$  years) and 50 healthy controls (male, aged  $59 \pm 8.01$  years) was acquired. Scanning was done using a 3T GE Discovery MR750 MRI and a 32-channel head coil. 3D T1-weighted fSPGR and 3D pseudocontinuous ASL (pCASL) scans acquired. The pCASL scans were processed using ExploreASL to produce spatial covariance (CoV) CBF quantification [2,3]. Twelve concussion-related regions-of-interest (ROIs) were selected from the Harvard-Oxford (HO) and Hammers (HS) Atlases [4]. Fifty-one left and right ROIs using rCBF and ASL sCoV data were included in a group-wise Mann-Whitney U statistical analysis. Pearson's r correlations were performed with significantly abnormal ROI data from CFL subjects and their demographic and neuropsychological data.

**Results:** Ninety-one significantly abnormal ROIs were calculated. Four ROIs were bilaterally abnormal with CBF and ASL sCoV methods. Three of the four ROIs had significantly elevated CBF relative to the healthy controls, but all four had significantly reduced ASL sCoV. The superior parietal gyrus had the most significant correlations, and elevated CBF and ASL sCoV seemed to be correlated with a more aggravated concussion history and worsened neuropsychological scores.

**Conclusions:** We were able to perform personalized evaluation of each former player. This is critically important because the forces (direction, number, amplitude, etc.) would be unique to each person. Using MRI-based blood flow measures using pCASL microvascular dysregulation was clearly present and may have been related to repetitive head impacts sustained decades earlier.

P144

# The Influence of Age and Sex on Resting State fMRI (rs-fMRI) Signal Temporal Complexity

N. Simard <sup>1</sup>, S. Ulmer <sup>2</sup> and M. Noseworthy <sup>1</sup><sup>1</sup> McMaster University; Canada<sup>2</sup> neurorad.ch, Switzerland

**Aim:** Because of its richness MRI data is becoming increasingly used in machine learning (ML) studies. Understanding the relationship of healthy aging on quantitative MRI data can improve design/execution of ML algorithms for detecting/grading of neuropathology. With the evolution of large-scale data repositories (IDA, HCP, NITRC, UK BIOBANK, etc.) [1–4], it is imperative to evaluate the effects of sex and healthy aging on quantitative MRI metrics. Resting state fMRI (rs-fMRI) temporal complexity (TC) has shown value where a reduction correlates with reduced function. Our aim was to assess the effect of

age and sex on TC over brain regions of interest (ROIs) as defined by the Julich Histological Atlas (JHA).

**Methods:** To assess functional complexity, over 10,000 healthy control 3T datasets (males and females between the ages of 18–70) were downloaded from open-source data repositories. A minimum of ( $n = 88$ ) for ages 30, 50, and 60 years old, sex matched, were collected to satisfy Cochran's formula for 95% sensitivity with regards to complexity analysis. A home-built python processing pipeline facilitated the voxel-wise complexity analysis by calculating a voxel's temporal fractal dimension [5–8]. Gray matter regions of interest (ROIs) were then segmented in reference to the JHA and evaluated for age and sex [9].

**Results:** A one-way ANOVA identified significant age effects ( $p = 0.03058$ ) on TC. The standard deviations for each age group and ROI show there are significant differences in the 30-year-old group ( $p = 0.0198$ ). However, there are limited differences in variability in TC between 50 and 60 year olds. These standard deviations also support the idea that there is increased variability in TC with age. Also we noted differences in mean TC values between males and females in the 30 and 60 year old age groups ( $p = 0.000623$ ), implying that healthy women have higher brain TC compared to healthy men in these age groups. The caveat to this finding is that women also demonstrate a higher amount of variance compared to men, as demonstrated by the ANOVA of TC standard deviations for each age group, ROI, and sex ( $p = 0.001649$ ).

**Conclusions:** Brain rs-fMRI temporal complexity is influenced by both sex and age. These factors must be considered when using 'Big Data' in ML models with quantitative brain MRI. More in-depth statistical investigation is required to establish specific relationships between altered temporal functional complexity with aging and sex.

P145

### Hemodynamic Assessment of Internal Carotid Artery Aneurysms Based on 3D TOF MRA Signal Intensity and Spatial Distribution: a Comparative Study with 4D Flow MRI

C. Santarosa, O. Brina, P. Reymond, K. Lovblad and M. I. Vargas

HUG Hôpitaux Universitaires Genève, Switzerland

**Aims:** Hemodynamics of cerebral aneurysms may be related to aneurysm instability. In routine clinical practice, 3D TOF MRA is used for the detection and morphological characterization of brain aneurysms. As 3D TOF MRA is based on flow-related enhancement, it might allow deriving some aneurysm hemodynamic properties too. We, therefore, evaluated whether the aneurysm TOF signal intensity and spatial distribution were associated with the aneurysm flow patterns and velocity, as determined with 4D flow MR imaging.

**Methods:** A consecutive series of 30 patients with internal carotid artery aneurysm have been considered. These patients underwent a 3D rotational angiography (3DRA) and an MRI examination, including 4D flow MRI and 3D TOF MRA. 4D flow MRI velocity field data and 3D TOF MRA signal intensity data were combined with a vascular geometric scaffold derived from the 3DRA. Paraview software (<http://paraview.org/>) was used to depict flow patterns through streamlines and analyze the spatial distribution of 4D flow MRI velocities and 3D TOF signal intensity.

**Results:** Within the volume of each aneurysm, a moderate association between 3D TOF signal intensities and 4D flow velocities was found (mean Pearson correlation coefficient = 0.567,  $p < 0.05$  for all aneurysms). In all aneurysms, 3D TOF MRA allowed characterizing the inflow jet as diffuse versus concentrated correctly. The aneurysm TOF signal intensity relative to the parent vessel was significantly lower in the 12 aneurysms with a complex



flow pattern, having more than one vortex core or no visible vortex core, than in the 18 aneurysms with a simple flow pattern, having a single vortex core ( $p < 0.05$ ).

**Conclusions:** A routine 3D TOF MRA, besides the appreciation of the morphology of the aneurysm, may allow inferring some of its hemodynamic properties, especially concerning the inflow jet and the flow pattern complexity.

P146

### Improving Sensitivity in mTBI Imaging of Individual Patients—Beyond Conventional MR Imaging. A Case-Control-Study

S. Ulmer <sup>1</sup>, A. Palla <sup>2</sup>, C. Fuchs <sup>3</sup>, N. Simard <sup>4</sup> and M. D. Noseworthy <sup>5</sup>

<sup>1</sup> neurorad.ch, Switzerland

<sup>2</sup> Swiss Concussion Center, Schulthess Clinic, Switzerland

<sup>3</sup> SportClinic Zürich, Switzerland

<sup>4</sup> TBIFinder, Canada

<sup>5</sup> St. Joseph's Healthcare Hamilton, McMaster University, Canada

**Aim:** The gold standard to depict posttraumatic brain change is susceptibility weighted MR imaging (SWI) at 3 T. However, SWI only detects residual blood products and is insensitive to microstructural or physiologic damage i.e., caused by blunt head trauma—despite persistent patient symptoms. We report on a novel way to identify and grade post-traumatic brain lesions using MRI resting state functional MRI (fMRI) and diffusion tensor imaging (DTI). For over 2 decades now, DTI has also been used in brain trauma imaging in professional athletes of collision sports.

**Methods:** Our patient is a 16 yo junior national ice hockey player with a history of recurrent blunt head traumas caused by various “bodychecks”, three times with loss of consciousness. Following the most recent “bodycheck” in 2/2021 he complains about headaches, attention disorder, fatigue, visual problems in reading, slight right leg weakness, and gait disturbances. Conventional 3 T MRI including SWI is normal.

MRI was performed using a 3 T Ingenia (Philips, The Netherlands) using a 16-channel head coil including resting state fMRI (TR/TE = 2000/35 ms,  $3 \times 3 \times 3$  mm) and DTI (60-direction;  $b = 1000$  s/mm<sup>2</sup>; TR/TE = 10'000/87 ms,  $3 \times 3 \times 3$  mm). TBIFinder™ software was used to calculate a temporal complexity metric (from resting state fMRI) and diffusion tensor metrics (FA, RD, AD, MD) for each brain region, based on the MNI-standard space. The software provides personalized analysis (age/sex matched) through a regional Z-score based on a database of almost 17,000 healthy brains. A standard deviation (SD) of  $>2.5$  from healthy controls was considered clinically relevant.

**Results:** The most striking changes were found in the right visual cortex (V5,  $>5$  SD) followed by the right inferior parietal lobule ( $>3.5$  SD) in rs-fMRI. Infratentorial the right Crus I was 2.9 SD off healthy controls. Most prominent findings in DTI ( $>3$  SD) were located in the left optic radiation, followed by the right optic radiation ( $>2.5$  SD). Changes of  $>2.5$  SD were depicted in the left cortico-spinal tract, left uncinate fascicle and left superior longitudinal fascicle. Infratentorial there were changes of 2SD from normal in the right lobule V, VI and the left lobule VI.

**Conclusions:** All symptoms could be explained by our imaging findings. Conventional MRI at 3 T is not sensitive enough to depict damage to the brain, thus this advanced imaging protocol should be an add-on for inconclusive MRI.

P147

### Analysis of Anatomical Distribution of Middle Cerebral Artery M2 Segment Vessel Occlusions and Its Cortical Branches in Acute Ischemic Stroke Patients

P. Gruber, P. Valbuena, R. Sassenburg, J. Anon, L. Anderegg, J. Berberat and L. Remonda

Kantonsspital Aarau AG, Switzerland

**Aim:** Medium Vessel occlusions (MeVOs) makes up to 25–40% of all acute stroke cases. There is an on-going debate, whether and how to treat MeVOs. Anatomical considerations are of importance for both the treatment plan and outcome. Thus, we analyzed the anatomical distribution of middle cerebral artery M2 (MCA-M2) segment occlusion and its subsequent cortical branches (CB) in acute ischemic stroke patients (AIS) at our stroke center.

**Methods:** Retrospective, mono-centric analysis of radiological and clinical data of acute ischemic stroke (AIS) patients with MCA-M2 segment occlusion with regard to the anatomic distribution of MCA-M2 occlusion and its subsequent CB.

**Results:** A total of 203 patients with median age 77 (IQR 66–83) years were included. There was an equal number of right vs. left sided MCA-M2 vessel occlusions (right:  $n = 97$ , left:  $n = 106$ ) observed. Median number of affected MCA-M2 cortical branches was 4 (IQR, 3–6). Median NIHSS Score on admission was 9 (3–15). For both hemispheres, CB of the inferior trunks were significantly more affected than the superior trunks. Endovascular treatment (EVT,  $n = 94$ ) was associated with a significant better outcome compared to patients with medical management alone ( $p = 0.027$ ).

**Conclusions:** In this cohort of acute MCA-M2 segment occlusions, inferior trunks were significantly more affected compared to the superior trunks. The subsequent cortical branches of the paracentral region of both hemispheres were more commonly involved. In eloquent vascular territories, EVT was more often performed.

P148

### CSF Flow in the Optic Nerve Subarachnoid Space Applying Diffusion Imaging in Patients with Idiopathic Intracranial Hypertension

J. Berberat <sup>1</sup>, P. Gruber <sup>1</sup>, L. Remonda <sup>1</sup> and H. Killer <sup>2</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> University of Basel, Switzerland

**Introduction:** The ophthalmologic hallmark of idiopathic intracranial hypertension (IIH) is papilledema (PE), which if untreated can lead to damage of the visual field, visual acuity and even legal blindness. A clear indicator for this is impaired CSF dynamics in a compartmentalized subarachnoid space (SAS) of the optic nerve (ON).

The purpose of this study was to examine the CSF flow rates in the SAS of the ON and the brain in patients with IIH compared to controls by applying non-invasive diffusion-weighted MRI.

**Methods:** A retrospective analysis of diffusion-weighted MR images of 5 patients with IIH (10 ONs), mean age:  $31 \pm 10$  years (5 women), and 11 healthy controls (22 ONs, mean age:  $60 \pm 13$  years, 5 women) was performed. The flow velocity flow-range ratio (FRR) between the intracranial cavity and the SAS of the ON was calculated in both groups.

**Results:** The mean FRR was  $0.55 \pm 0.08$  in patients with IIH and  $0.63 \pm 0.05$  in healthy controls. The difference between patients with IIH and healthy controls was statistically significant ( $p < 0.05$ ).

**Summary:** In IIH, the vision loss is the most feared complication. The pathophysiology of IIH is not fully understood, but is strongly linked to a reduced uptake of CSF into the central dural sinus veins. The knowledge about the flow ratio of CSF may be of clinical relevance for the treatment decisions of IIH, medical or surgical. As the primary goal of treatment is to prevent the loss of vision and visual field, it is important to know whether the communication of CSF between the intracranial CSF and the CSF in the perioptic space is intact. The reduced CSF flow demonstrated in this study by the IIH patients compared to controls might be involved in the pathophysiology of IIH, and diffusion-weighted MRI can be a useful non-invasive tool to study the CSF flow dynamics within the SAS ON.

**Conclusions:** The CSF flow velocity was decreased in patients with IIH with PE compared to controls. The knowledge about the flow ratio of CSF may be of clinical relevance for the treatment decisions of IIH and diffusion-weighted MRI can be a useful non-invasive tool to study the CSF flow dynamics within the SAS ON.

P149

### Early Cervical Spondylotic Myelopathy Prediction Using Dynamic Diffusion MR Imaging

J. Berberat <sup>1</sup>, L. Anderegg <sup>2</sup>, A. R. Fathi <sup>3</sup>, P. Gruber <sup>1</sup>, O. Hausmann <sup>4</sup> and L. Remonda <sup>1</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> Kantonsspital Aarau, Switzerland

<sup>3</sup> Hirslanden Klinik Aarau, Switzerland

<sup>4</sup> St. Anna Hospital, Germany

**Introduction:** Cervical spondylotic myelopathy (CSM) is the most common form of chronic spinal cord injury in adults; yet, the epidemiology is poorly understood due the difficulties in diagnosis. Intramedullary hyperintensity (IHIS) on T2w. imaging has only a sensitivity of 60% for the detection of clinical myelopathy compared to a sensitivity of 80% for increased intramedullary apparent diffusion coefficient (ADC) values. Diffusion tensor imaging (DTI) in flexion-extension has been shown to improve the diagnosis of CSM [1,2]. The purpose of this study was to examine whether the MR in extension-flexion combined with T2w. imaging and DTI parameters can provide a more accurate diagnosis in early stages of clinical myelopathy.

**Methods:** Patients with symptomatic CSM were examined in maximum neck flexion-extension in a 3T MRI and allocated into two age-matched groups: i) patients with visible IHIS on T2w. imaging (IHIS+, n = 10, 55 ± 11 y) and ii) patients without IHIS (IHIS-, n = 11, 59 ± 14 y). Range of motion, space available for the spinal cord and diffusion parameters (ADC, AD, RD, FA) were measured and compared between the neck positions and between both groups, respectively.

**Results:** Statistically significant differences based on paired *t*-test between the control (C2/3) and the pathological segments were found for IHIS+ group at normal neck position in AD; at flexion in ADC and AD; and at extension in ADC, AD and FA values. For the IHIS- group, statistically significant differences between the control (C2/3) and the pathological segments were found at extension in ADC values. When comparing ADC, AD, RD, and FA values between the IHIS- and IHIS+ groups, statistically significant differences were found in RD in all 3 neck positions.

**Conclusions:** Statistically significant increase in ADC values between the control and the pathological segments were found for IHIS+ and IHIS- groups in extension only. Our finding suggests that ADC at extension may serve as an identification of early onset for myelopathy: ADC values are high at early on myelopathy and lower in the later stages. When the white matter tracts are disrupted or the permeability of axonal membranes is increased, the ADC will increase. Cord compression in extension may further provoke increased membrane permeability and therefore lead to increased ADC values. In

addition, increase in ADC may indicate potentially reversible spinal cord injury and support the indication for surgery in selected cases.

P150

### Quantitative Susceptibility Mapping Using MRI in Adults with Attention-Deficit Hyperactivity Disorder and Healthy Controls—Iron Load as a Potential Sign of Accelerated Aging?

J. Berberat <sup>1</sup>, C. Späni <sup>2</sup>, S. Romer <sup>2</sup>, P. Stämpfli <sup>2</sup>, X. Li <sup>3</sup>, J. Hua <sup>3</sup>, P. van Zijl <sup>3</sup>, K. Lövblad <sup>1</sup>, E. Seifritz <sup>2</sup>, B. B. Quednow <sup>2</sup> and P. G. Unschuld <sup>1</sup>

<sup>1</sup> University Hospitals of Geneva and University of Geneva; St. Anna Hospital

<sup>2</sup> PUK Zürich; St. Anna Hospital

<sup>3</sup> John Hopkins University, USA

**Introduction:** Attention-deficit hyperactivity disorder (ADHD) may result from disrupted neural brain development including a high degree of interdependence between the development of neural and vascular brain structures. By using the quantitative susceptibility mapping (QSM) technique, this study aimed to compare iron depositions between ADHD adults and healthy controls and hypothesized that ADHD might be closely associated with a known risk of increased cerebral small vessel disease (cSVD) [1,2].

**Methods:** Middle-aged adults with ADHD and controls underwent 3T MRI examination, standardized psychometric exploration and assessment of lifestyle factors. The QSM maps were calculated using the QSMxT framework and Hochberg correction was used for multiple comparisons. An unpaired *t*-test was used to detect possible statistically significant differences in iron content between ADHD patients and healthy volunteers. ANOVA was executed to detect a possible connection with cSVD risk factors such as BMI, age, smoking habits, and alcohol consumption and the local iron contents.

**Results:** Susceptibility changes in ADHD patients ( $n = 32$ ,  $35 \pm 10$  y) and healthy volunteers ( $n = 29$ ,  $32 \pm 12$  y) were obtained from QSM analysis. Statistically significant increases ( $p < 0.05$ ) in iron content were found ADHD vs. controls in several brain areas, such as caudate, precuneus, precentral gyrus, cerebral white matter, cingulate gyrus, supramarginal gyrus, accumbens area, pars opercularis, parietal lobule, parahippocampal gyrus, isthmus cingulate gyrus and lateral occipital gyrus. ANOVA revealed no statistically significant connection with the QSM values and lifestyle factors. No statistically significant differences were found between the life style factors when comparing the groups.

**Discussion:** Increased susceptibility values in several brain structures were detected when comparing iron content in middle-aged adults with and without ADHD. This might relate ADHD to known increased cSVD at middle age. The existence of silent cSVD as a major risk factor of cerebrovascular brain damage opens the possibility that adult ADHD patients may represent a clinical phenotype associated with increased risk for early onset vascular disease, given the well-established relationship between cardiovascular disease, cSVD, and impaired mental health in old age. Therefore, middle-aged adults with ADHD might be at greater risk for aging-related disorders and QSM may serve as a biomarker for early onset vascular disease.

## P151-YouClin

**Visualization of Intracranial Aneurysms Treated with Woven EndoBridge (WEB) Devices Using Ultrashort Echo Time Magnetic Resonance Imaging (UTE-MRI)****D. Toth**<sup>1</sup>, **S. Sommer**<sup>2</sup>, **I. Barnaure**<sup>1</sup>, **J. Madjidyar**<sup>1</sup>, **P. Thurner**<sup>1</sup>, **Z. Kulcsar**<sup>1</sup> and **T. Schubert**<sup>1</sup><sup>1</sup> Universitätsspital Zürich, Switzerland<sup>2</sup> Siemens Healthineers AG, Switzerland

**Aims:** Assessing treatment success of intracranial aneurysms with Woven EndoBridge (WEB) devices using MRI is important in follow-up imaging. Depicting both the device conformation as well as any reperfusion is challenging due to susceptibility artefacts. We demonstrate the usefulness of contrast-enhanced 3D-Ultrashort Echo-Time (UTE) sequence in this setting.

**Materials and Methods:** 21 MRIs performed after WEB treatment, in 11 patients (8 females) with a total of 13 treated aneurysms (6 anterior communicating, 5 basilar, 2 medial cerebral arteries) were prospectively included. All MRIs were performed on the same 3-Tesla scanner. Two MRIs in one patient were excluded, due to additional surgical clipping. We compared the visualization of device configuration and reperfusion in 3D isotropic UTE-MRI post contrast (TR: 4.62, TE 0.04 ms) with standard time-of-flight (TOF) angiography without and with intravenous contrast, as well as DSA (available in 17 out of 19 cases). Two interventional radiologists rated the images separately and in consensus.

**Results:** Visualization of the WEB device position and conformation was rated as superior or highly superior using the UTE sequence in 18/19 MRIs and equal in 1, compared to TOF. Reperfusion was visible in 7/17 cases in DSA. TOF was able to grade reperfusion correctly in 13 cases and UTE in all 17 cases. Of the two remaining cases without DSA correlation, one demonstrated neck reperfusion on UTE, but not on TOF.

**Conclusions:** Contrast-enhanced UTE is a novel MRI sequence that shows added value to standard sequences in non-invasive and radiation-free follow-up imaging of intracranial aneurysms treated using a WEB device.

## P152

**Unusual Complication in Skull Base Fracture Management—A Case Report****D. Valsecchi, M. Giamundo, P. Ahlborn and C. Zweifel**

Kantonsspital Graubünden, Switzerland

**Background:** Skull base fractures are often associated with CSF fistulas and otorrino-liquorrhoea requiring surgical correction.

We report here the case of a patient victim of craniofacial trauma who was treated surgically with a pluridisciplinary approach and who presented the progressive development of an unusual iatrogenic Arnold-Chiari syndrome.

**Case report:** On 20 April 2022, the patient had been transported to our emergency units following concussive head and facial trauma from precipitation. The CT-scan detected complex fronto-basal fracture with opening of the frontal sinus and subarachnoidal post-traumatic hemorrhage. The patient reported auricular and retropharyngeal flow perception. Multidisciplinary surgical treatment was therefore planned throughout bicoronal access with reduction of the orbitofrontal fractures, direct osteosynthesis and bilateral skull base dural plasticity by means of temporal craniotomy. Postoperatively, an external spinal drain was placed to protect the plastic, with a set-up of 5–10 cc/h.

At day-3 postop, the external spinal drain was removed. On postoperative day 5 a subacute progressive neurological deterioration occurred, with savoury state (GCS 9/15)

and impaired deglutition, with necessary placing of a nasopharyngeal tube. An MRI showed two bilateral frontal subcentral hygromas, persistence of fluid collection in the paranasal sinuses, collapsing of the 4th ventricle and descent of the cerebellar tonsils 3 mm below McRae's line. An MRI of the lumbar spine showed no signs of pseudomeningocele. After exclusion of infectious or epileptic causes, a spinal 'blood patch' and a reinforcement of the cranial base plastic with application of nasal swabs were empirically performed. After 24 the patient presented a clinical improvement with GCS 13/15.

**Discussion:** The hypothesis put forward sees a possible acute hypotonic syndrome from combined spinal and nasal loss, on probable persistence of the small dural fistula. Only once both lesions were corrected, although not clearly visualised on MRI, was there clinical improvement.

**Conclusions:** A preliminary radiological study could have focused on any previous signs of a small posterior fossa, putting in place any underlying risks. By neurological worsening after placing of a spinal drain, a new brain imaging should be performed in the aim to check for posterior fossa signs of compression. If a likely persistent fistula is considered, empirical treatment could be discussed and performed.

P152

### Large-Scale Morphometry of the Subarachnoid Space in the Optic Nerve: A Functional Exchange Surface Area of the Meningothelial Cells

D. Rossinelli <sup>1</sup>, H. Killer <sup>2</sup>, P. Meyer <sup>3</sup>, G. Knott <sup>4</sup>, G. Fourestey <sup>4</sup>, C. Kohler <sup>2</sup>, A. Neutzner <sup>2</sup>, P. Gruber <sup>1</sup>, L. Remonda <sup>1</sup>, V. Kurtcuoglu <sup>5</sup> and J. Berberat <sup>1</sup>

<sup>1</sup> Kantonsspital Aarau, Switzerland

<sup>2</sup> University Hospital Basel and University of Basel, Switzerland

<sup>3</sup> University Hospital Basel, Switzerland

<sup>4</sup> Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland

<sup>5</sup> University of Zurich, Switzerland

**Background:** The subarachnoid space of the optic nerve contains a variety of trabeculae, septae and pillars. The arachnoid and the pia mater are all covered with meningotheelial cells (MECs) that act as a barrier between the cerebrospinal fluid and the parenchyma of the optic nerve. MECs are multifunctional cells, capable of phagocytosis as well as secretion of various biochemical substances. They thereby contribute to the homeostasis of the microenvironment of the optic nerve. As they provide a functional exchange surface, the total area which they cover is of high importance in order to estimate their effect as a cerebrospinal fluid clearing system.

**Methods:** We carried out volumetry and morphometry of a human optic nerve section, at the pixel resolution of 0.325  $\mu\text{m}$  using tomographic microCT. Segmentation was performed by leveraging supercomputers.

**Results:** The optic nerve subarachnoid space (ON SAS) microstructure is shown to amplify the MECs surface area up to 5-fold compared to an SAS ON devoid of internal structures, by just occupying 34% of the total volume. We identified 61 "compartments" with a diameter larger than 130  $\mu\text{m}$  and volumes between  $10^{-1}$  and  $10^{-3}$   $\text{mm}^3$ .

**Conclusions:** This morphometric study provides for the first time an estimation of the interface area of CSF and MECs and assessed a methodology to characterize and quantify compartmentalization of the ON SAS. Accurate quantification on this functional exchange surface area is of high importance for estimating their performance as a CSF clearing system in optic nerve subarachnoid space.

P153

## Sex Differences in Outcomes of Intravenous Thrombolysis in Acute Ischemic Stroke Patients with Preadmission Use of Antiplatelet Agents: A Population-Based Study of the Swiss Stroke Registry

R. Nosedà <sup>1</sup>, F. Rea <sup>2</sup>, A. Pagnamenta <sup>3</sup>, P. Agazzi <sup>4</sup>, G. Bianco <sup>4</sup>, S. Sihabdeen <sup>4</sup>, D. Seiffge <sup>5</sup>, P. Michel <sup>6</sup>, K. Nedeltchev <sup>7</sup>, L. Bonati <sup>8</sup>, G. Kägi <sup>9</sup>, J. Niederhauser <sup>10</sup>, T. Nyffeler <sup>11</sup>, S. Wegener <sup>12</sup>, L. Schelosky <sup>13</sup>, F. Medlin <sup>14</sup>, B. Rodic <sup>15</sup>, N. Peters <sup>16</sup>, S. Renaud <sup>17</sup>, M. Mono <sup>18</sup>, E. Carrera <sup>19</sup>, U. Fischer <sup>8</sup>, R. Nosedà <sup>1</sup> and C. Cereda <sup>20</sup>

<sup>1</sup> Division of Clinical Pharmacology and Toxicology, Institute of Pharmacological Sciences of Southern Switzerland, Ente Ospedaliero Cantonale, Lugano, Switzerland

<sup>2</sup> Unit of Biostatistics, Epidemiology and Public Health, Department of Statistics and Quantitative Methods, University of Milano-Bicocca, Milan, Italy

<sup>3</sup> Clinical Trial Unit, Ente Ospedaliero Cantonale, Lugano, Switzerland

<sup>4</sup> Neurocenter of Southern Switzerland, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, Switzerland

<sup>5</sup> University Hospital Bern, Department of Neurology, Bern, Switzerland

<sup>6</sup> Lausanne University Hospital, Stroke Center, Neurology Service, Lausanne, Switzerland

<sup>7</sup> Kantonsspital Aarau, Department of Neurology, Aarau, Switzerland

<sup>8</sup> University Hospital Basel and University of Basel, Department of Neurology and Stroke Center, Basel, Switzerland

<sup>9</sup> Kantonsspital St. Gallen, Department of Neurology, St. Gallen, Switzerland;

<sup>10</sup> Stroke Unit, Hopital Nyon, Switzerland

<sup>11</sup> Luzerner Kantonsspital, Center of Neurology and Neurorehabilitation, Luzern, Switzerland

<sup>12</sup> Universitätsspital Zürich, Neurology, Zürich, Switzerland

<sup>13</sup> Kantonsspital Münsterlingen, Division of Neurology, Münsterlingen, Switzerland

<sup>14</sup> HFR Fribourg, Stroke Unit, Division of Neurology, Fribourg, Switzerland

<sup>15</sup> Kantonsspital Winterthur, Neurology, Winterthur, Switzerland

<sup>16</sup> Hirslanden Hospital, Department of Neurology and Stroke Center, Zurich, Switzerland

<sup>17</sup> Pourtalès Hospital, Division of Neurology, Neuchâtel, Switzerland

<sup>18</sup> Stadtsipital Waid und Triemli, Stroke Unit, Zürich, Switzerland

<sup>19</sup> Hôpitaux Universitaires de Genève, Department of Neurology, Geneva, Switzerland

<sup>20</sup> Neurocenter of Southern Switzerland, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, Switzerland

**Aims:** Clinical outcomes of intravenous thrombolysis (IVT) in acute ischemic stroke (AIS) rely on patient individuality, which includes biological sex. Since a patient's sex may influence platelet function, women and men with AIS could respond differently to IVT treatment depending on preadmission use of antiplatelet agents. We aimed to compare safety and efficacy outcomes of IVT between women and men with AIS in relation to preadmission use of antiplatelet agents.

**Methods:** Multicentre non-concurrent population-based study (Swiss Stroke Registry (SSR)).

Consecutive patients admitted from 1 January 2014, to 31 January 2020, to hospitals participating in the SSR presenting with AIS and receiving IVT without endovascular treatment. Patients who used anticoagulants before admission were excluded. The study population was divided into two groups based on the patient's sex and thereafter compared in terms of preadmission use of antiplatelet agents. The primary safety outcome was in-hospital symptomatic intracerebral haemorrhage (sICH). The primary efficacy outcome was functional independence (FI) at 3 months after discharge

**Results:** The study cohort included 4996 patients (2124, 43%, women, older than men, median age 79 versus 71 years,  $p < 0.0001$ ). Comparable proportions of women (39.92%) and men (40.39%) used antiplatelet agents (single or dual) before admission ( $p = 0.74$ ). 136 (2.72%) patients presented in-hospital sICH, with similar odds between women and men (adjusted odds ratio, AOR, 0.96, 95%CI 0.65–1.43). No interaction was found between sex of patients and preadmission use of either single or dual antiplatelet agents in relation to in-hospital sICH ( $p = 0.86$  and  $p = 0.21$ , respectively). Men had higher odds of FI at 3-

months (AOR 1.35, 95%CI 1.10–1.66), regardless of preadmission use of antiplatelet agents (values of interaction between sex of patients and preadmission use of either single or dual antiplatelet agents  $p = 0.41$  and  $p = 0.62$ , respectively).

**Conclusions and Relevance:** No sex differences were observed in the safety of IVT in AIS patients regarding pre-admission use of antiplatelet agents. Men showed more favourable 3-month FI than women following IVT; however, this sex difference was apparently not explained by a sex-specific mechanism related to preadmission use of antiplatelet agents.

P154

### Symptoms and Patterns of Symptom Propagation in Incipient Ischemic Stroke and Migraine Aura

A. Scutelnic <sup>1</sup>, J. Bracher <sup>1</sup>, J. Bracher <sup>1</sup>, L. Kreis <sup>1</sup>, M. Beyeler <sup>1</sup>, U. Fischer <sup>2</sup>, M. Arnold <sup>1</sup>, H. Mattle <sup>1</sup>, S. Jung <sup>1</sup> and C. Schankin <sup>1</sup>

<sup>1</sup> Inselspital—Universitätsspital Bern—Universitätsklinik für Neurologie, Switzerland

<sup>2</sup> Department of Neurology, University Hospital Basel and University of Basel, Basel, Switzerland

**Background and objectives:** A detailed history of focal neurological deficits is important for the differential diagnosis of incipient ischemic stroke and migraine aura. The aim of our study is to describe in detail the symptom type, the patterns of symptom spreading, the patterns of symptom succession and the time lapse between symptoms in patients with ischemic stroke and migraine with aura.

**Methods:** Using a structured questionnaire we interviewed consecutive patients with ischemic stroke and migraine with aura. Stroke diagnosis was confirmed by imaging and migraine with aura was diagnosed according to the current criteria of the International Headache Society. Wake-up strokes and patients with severe cognitive deficits have been excluded.

**Results:** In stroke patients and migraine patients respectively, 50/78 (64.1%) vs. 123/326 (37%) had one visual symptom, 18 (23%) vs. 127 (38%) two visual symptoms, 5 (6%) vs. 69 (21%) three visual symptoms, 2 (2%) vs. 4 (1%) four visual symptoms and 3 (3%) vs. 3 (1%) five visual symptoms. In stroke patients and MwA patients respectively, 76/145 (52.4%) vs. 116/175 (66%) reported paresthesia and 92/145 (63.4%) vs. 132 (75%) numbness. In stroke and MwA patients respectively, 23/117 (19.6%) vs. 146 (72.6%) had visual symptoms as first occurring symptom, 34 (29%) vs. 28 (13.9%) sensory symptoms, 14 (11.9%) vs. 14 (6.9%) speech disturbance, 25 (21.3%) vs. 2 (0.9%) motor symptoms, 3 (2.5%) vs. none vertigo, one (0.8%) vs. none ataxia, 17 (14.5%) vs. 9 (4.4%) two or more symptoms occurring simultaneously. In stroke and MwA respectively, in 85/107 (79.4%) vs. 223 (94%) the next consecutive symptom occurred within 60 min, in 1 (0.9%) vs. 11 (4.6%) within 120 min, and in 2 (1.8%) vs. 1 (0.4%) within 180 min. In stroke and MwA patients respectively, 23/117 (19.6%) vs. 146 (72.6%) had visual symptoms as first occurring symptom.

**Conclusions:** There is a significant number of stroke patients with migraine-like symptoms and migraine with aura patients with stroke-like symptoms. Our findings expand the clinical spectrum of ischemic stroke and migraine with aura.

P155

### Cerebral Hemodynamics during Early Verticalization after Successful Thrombectomy Post Stroke (CHEST-Study)

J. Deseö <sup>1</sup>, A. Schwarz <sup>1</sup>, T. Pipping <sup>1</sup>, A. R. Luft <sup>2</sup>, S. Wegener <sup>3</sup> and J. P. Held <sup>4</sup>

<sup>1</sup> University and University Hospital of Zurich, Department of Neurology, Switzerland

<sup>2</sup> University and University Hospital of Zurich, Department of Neurology \ \ Clinical Neuroscience Center, University of Zurich \ \ cereneo Center for Neurology and Rehabilitation, Switzerland



<sup>3</sup> University and University Hospital of Zurich, Department of Neurology \ \ Clinical Neuroscience Center, University of Zurich, Switzerland

<sup>4</sup> University and University Hospital of Zurich, Department of Neurology \ \ Rehabilitation Center Triemli Zurich, Valens Clinics, Switzerland

**Aims:** The immediate reestablishment of cerebral perfusion is one of the most important factors for recovery after ischemic stroke. Mechanical thrombectomy (MT) is an effective acute intervention for vessel recanalization. Usually, patients remain in supine position the first hours after MT. During verticalization, patients are brought up to 70° of tilt using an early mobilization aid. Early verticalization of patients after stroke could have a positive influence on rehabilitation outcome. However, if it alters cerebral blood flow in the affected territory is unknown. The aim of this study was to determine the association between verticalization and cerebral blood flow velocity (CBFV) in healthy subjects and in acute ischemic stroke patients within the 24 h after thrombectomy.

**Methods:** So far, twenty healthy subjects and six stroke patients after successful MT were included into this study. The study protocol included a stepwise verticalization in supine position on a tilt table device up to 70°, including a phase of head down tilt at −5°. CBFV was measured in the middle cerebral artery of the dominant hemisphere in healthy subjects and the affected hemisphere in stroke patients using a holter doppler device. Effects of increasing angles of verticalization on CBFV over time were assessed in a linear mixed effects model.

**Results:** All participants completed the protocol. For one patient, the duration at 70° was shortened due to reported headache and dizziness. Mean CBFV progressively decreased with increasing angles of verticalization in both healthy subjects and stroke patients. A mean decline in CBFV of  $4.8 \pm 4.3$  cm/s in healthy subjects and  $10.1 \pm 9.1$  cm/s in stroke patients was shown between lying supine and a 70° vertical position. The greater drop of CBFV in response to increasing angles of verticalization in stroke patients was shown to be significant in the linear mixed effects model ( $p = 0.005$ ).

**Conclusions:** Our data indicate that the change of CBFV during verticalization differs between patients post MT and healthy subjects. Post MT patients showed a greater decrease in CBFV at higher angles of verticalization. With inclusion of more patients, we anticipate a better understanding of the effects of verticalization on CBFV, and important insights regarding safety of mobilization post stroke and post MT.

P156

### Cerebral Microbleeds in Patients with Neurological Symptoms Associated with COVID-19: Distribution and Possible Pathophysiological Mechanisms.

A. Accorroni <sup>1</sup>, L. Sveikata <sup>1</sup>, M. Uginet <sup>1</sup>, G. Breville <sup>1</sup>, P. Stancu <sup>1</sup>, K. Lövlblad <sup>1</sup>, G. Allali <sup>2</sup> and F. Assal <sup>1</sup>

<sup>1</sup> Hôpitaux Universitaires de Genève (HUG), Switzerland

<sup>2</sup> Lausanne University Hospital and University of Lausanne, Switzerland

**Background and aims:** Cerebral microbleeds (CMB) emerged as a possible complication of COVID-19. We aimed to assess CMB presence, distribution, and potential underlying pathophysiological mechanisms in hospitalised COVID-19 patients.

**Methods:** In a cohort of 112 COVID-19 patients with neurological symptoms admitted to the Geneva University Hospital between March 2020 and May 2021, we assessed CMB distribution, and associations with clinical/radiological variables. Neuroimaging was performed on a 1.5 T MRI with susceptibility-weighted images, 3D time-of-flight angiography, and 3D-contrast-enhanced fat-saturated T1 black blood VISTA sequences. Two neurologists rated CMB using the Microbleed Anatomic Rating Scale and white matter hyperintensities using the Age-Related White Matter Changes score.

**Results:** 53 patients (47.0%) had CMB; in 45.3% of cases, CMB were found in lobar regions with a predilection for temporal (58.3%) and frontal (29.2%) lobes. Deep CMB were present in 18.9%, with corpus callosum CMB found in 15.0%, in 35.9% CMB distribution was mixed. CMB presence was not related to intubation, pulmonary involvement, nor to radiologic signs of endothelitis. Patients with CMB were more likely to have a higher burden of white matter hyperintensities (OR 1.13,  $p = 0.005$ , 95% CI: 1.03–1.24), to have hypertension as a comorbidity (OR = 2.34,  $p = 0.04$ , 95% CI: 1.04–5.30) and to suffer from an acute stroke during hospitalisation (OR: 3.50  $p = 0.012$ , 95% CI: 1.31–9.18).

**Conclusions:** In our sample, COVID-19 patients with neurological symptoms had a high burden of CMB. Their distribution suggests that they may be related to cardiovascular risk factors and cerebral amyloid angiopathy. CMB were also associated with an increased risk of acute stroke.

P157

### Impact of Cerebral Microbleeds in Stroke Patients with Atrial Fibrillation taking antithrombotics: a sub-analysis from the Microbleeds International Collaborative Network (MICON)

A. Zietz <sup>1</sup>, Y. Soo <sup>2</sup>, B. Yiu <sup>2</sup>, V. Mok <sup>2</sup>, T. Leung <sup>2</sup>, W. Chu <sup>2</sup>, J. Abrigo <sup>2</sup>, A. Polymeris <sup>1</sup>, D. Seiffge <sup>3</sup>, P. Lyrer <sup>1</sup>, J. Best <sup>4</sup>, D. Werring <sup>4</sup>, S. Engelter <sup>5</sup> and N. Peters <sup>6</sup>

<sup>1</sup> University Hospital Basel and University of Basel, Switzerland

<sup>2</sup> The Chinese University of Hong Kong, China

<sup>3</sup> Inselspital University Hospital and University of Bern, Switzerland

<sup>4</sup> Stroke Research Centre UCL Queen Square Institute of Neurology, Switzerland

<sup>5</sup> Department of Neurology, University Hospital Basel and University of Basel and Neurology and Neurorehabilitation, University Department of Geriatric Medicine Felix Platter, Switzerland

<sup>6</sup> Stroke Center, Klinik Hirslanden, Zürich, Switzerland

**Background and aims:** Cerebral microbleeds (CMB) are associated with increased risk of stroke. We aimed to evaluate the risk of intracerebral haemorrhage (ICH) and ischaemic stroke (IS) in patients with atrial fibrillation (AF) and CMB receiving different antithrombotic treatment regimes.

**Methods:** We performed a sub-analysis of patients with AF from the MICON pooled individual patient data cohort. The association of CMB burden (0, 1, 2–4, 5–10 and  $\geq 11$  CMB) with risks of subsequent ICH and IS in AF patients receiving different antithrombotics were analyzed with multivariable Cox regression.

**Results:** Among the 7379 patients with AF CMB were present in 2142 (27.3%). 3244 patients received a Vitamin K antagonist (VKA), 1981 a direct oral anticoagulant (DOAC), 626 an antiplatelet and 1528 a combination of anticoagulant plus antiplatelet (i.e., combination therapy). The incidences for both ICH and IS were higher in patients with CMB. Mainly pure deep CMB (aHR 4.21 [2.4–7.36]) and mixed deep CMB (aHR 2.95 [1.43–6.08]) were associated with ICH. The absolute incidence of IS was higher than ICH for most patients, except for the following treatment groups: (i) VKA with 5–10 CMB (25 per 1000 patient-years for ICH vs. 23 per 1000 patient-years for IS); (ii) combination therapy with 2–4 CMB (25 per 1000 patient-years for ICH vs. 12 per 1000 patient-years for IS); and (iii) combination therapy with  $\geq 11$  CMB (94 per 1000 patient-years for ICH vs. 48 per 1000 patient-years for IS).

**Conclusions:** For patients with AF with high burden of CMB receiving VKA or combination therapy were associated with increased risk of ICH, which approximated that of IS. Minimizing duration of a combination therapy according to recent guidelines and verifying the indication of the latter should be considered in AF related stroke patients with CMBs.

P158

### Detection Rates of Atrial Fibrillation by Prolonged Rhythm Monitoring with or without Preselection by Biomarkers in Patients with Embolic Strokes of Undetermined Source a Single Center Experience

P. Dorin, R. Zubal, G. Kägi, N. Ehl and J. Vehoff

Kantonsspital St. Gallen, Switzerland

**Background:** Cryptogenic stroke (CS) makes up about one quarter of all ischemic strokes. ESUS defines a subset of CS with embolic stroke pattern and no evidence of major risk cardioembolic sources, significant atherosclerosis and lacunar stroke. Atrial fibrillation (AF) increases stroke risk by five and this risk increases with age. Secondary prevention in CS still is a challenge as there is little evidence concerning the optimal treatment strategy. Usually, antiplatelet therapy for patients with non-cardioembolic ischemic stroke is recommended. In this retrospective evaluation, we aim to evaluate the impact of our intensified strategy to find AF in Patients with ESUS.

**Methods:** Monocentric, retrospective data analysis of patients with ESUS between May 2019 and September 2021, fulfilling the ESUS criteria, with in-hospital rhythm monitoring for at least 24 h without evidence of AF, who received ambulatory extended, non-invasive patch ECG monitoring for 28–32 days. Comparison of detection rates with or without the use of biomarkers (age, MR-proANP, left atrial volume index (LAVI), supraventricular extrasystoles during 24 h Holter-ECG/atrial runs with >20 beats, additional chronic embolic infarct on MRI).

**Results:** Out of 186 patients, in 14 AF was detected by extended rhythm monitoring (7.53%). There were 7 AF-cases in each of the two groups (without further selection criteria: 94 Patients, 7.45% ; with selection criteria: 92 Patients, 7.61%).

**Conclusions:** The use of additional selection criteria for extended rhythm monitoring in ESUS patients did not increase the detection rate of AF in our cohort of patients.

P159-YouClin

### Cardiac Complications Following Cerebrovascular Disease

M. Rohner, C. Gebhard, A. Luft and S. Wegener

University Hospital Zurich, University of Zurich, Switzerland

**Aim:** Cardiac complications are a relevant problem after stroke. (1–3) The aim of this study was to compare the differences in cardiac findings after acute ischemic stroke (AIS), transient ischemic attack (TIA) and hemorrhagic stroke (HS) in patients without history of cardiac disease.

**Methods:** For this retrospective study we included 843 patients from the Swiss Stroke Registry: 685 patients with AIS, 110 with TIA and 48 with HS. Only patients without any previous cardiac disease, severe neurological disease or cardio-embolic origin of their cerebrovascular disease (CVD) were included. Additionally, at least one cardiac check-up within the year after disease onset was compulsory. We screened medical reports within the year following CVD onset and every new cardiac finding was extracted for further analysis. The cardiac findings were categorized according to which anatomical or functional part of the heart they arose from. We established the following categories: rhythmogenic, myocardial, valve disease, cardiovascular and abnormal blood pressure. The frequencies of every individual cardiac parameter and of all 5 parameter categories were analyzed for every CVD subgroup.

**Results:** Rhythmogenic findings were observed in 75.2% of AIS patients, 63% of TIA patients and 50.0% of HS patients ( $p < 0.001$ ). 58.4% of AIS patients, 52.7% of TIA patients

and 40% of HS patients showed findings affecting the myocardium ( $p = 0.027$ ). Abnormal blood pressure was most frequent in HS patients with 43.8% (and in 15.8% of TIA and 14.4% of AIS patients,  $p < 0.001$ ). 10.9% of TIA patients, 5.8% of AIS patients and 0% of HS patients showed new cardiovascular findings ( $p = 0.023$ ). The most common new individual findings consisted of (supra)ventricular extrasystole, diastolic heart failure, atrial tachycardia, left atrial enlargement and arterial hypertension.

**Conclusions:** In 4 out of 5 cardiac parameter categories, significant differences in terms of frequencies were detected within the CVD subgroups. When directly comparing AIS to TIA, cardiac parameter categories were similar, so that most differences arose from comparing HS to (transient) ischemia. We conclude that cardiac complications are frequent in patients with stroke and transient ischemia, even without prior cardiac problems or suspected cardiac etiology of stroke. Not only AIS patients, but also HS and TIA patients should receive routine cardiological check-ups, in search of relevant cardiac complications.

P160

### Nonverbal Memory Tests Revisited: Differential Influence of Executive Functions and Neuroanatomical Correlates

N. Mock <sup>1</sup>, C. Balzer <sup>2</sup>, K. Gutbrod <sup>3</sup>, L. Jäncke <sup>4</sup>, L. Bonati <sup>2</sup> and W. Trost <sup>2</sup>

<sup>1</sup> Universitätsspital Zürich, Switzerland

<sup>2</sup> Reha Rheinfelden, Switzerland

<sup>3</sup> Bern University Hospital (Inselspital), Switzerland

<sup>4</sup> Universität Zürich, Switzerland

The detection of right temporal lobe dysfunction with nonverbal memory tests has remained difficult in the past. One reason for this might be the potential influence of executive functions on memory performance. The aim of this study was to investigate the differential influence of executive functions on three classic nonverbal memory tests and to identify the neuroanatomical correlates of these tasks with lesion-symptom mapping (LSM).

In a relatively large cohort of 119 patients with first-time CVA, memory performance was assessed in three nonverbal memory tasks including the Nonverbal Learning and Memory Test for Routes (NLMT), the Rey Complex Figure Test (RCFT), and the Visual Design Learning Test (VDLT). We used regression-analysis to calculate the amount of variance explained by five executive tests for each of the three nonverbal memory tests. Akaike's Information criterion (AIC) was used to compare nested models for each memory test, one with and one without executive functions as additional predictors. Furthermore, we computed LSM to evaluate which brain structures are crucial for the three nonverbal memory tests.

Preliminary results showed that amongst the three nonverbal memory tests the impact of executive functions was most pronounced for the RCFT. Model comparison with AIC suggested that including the executive functions as additional predictors yielded a better model only for the RCFT, but not for the other two nonverbal memory tests. LSM analysis revealed for the RCFT critical right subcortical structures, such as the caudate nucleus and for the NLMT right temporal structures including the hippocampus. The VDLT did not reach significance in LSM analyses.

These results corroborate a differential influence of executive functions on three classic nonverbal memory tests, showing the strongest influence on RCFT performance. Confirmatively LSM results for RCFT involve caudate nucleus that is part of fronto-striatal loops supporting executive functioning. Moreover, LSM results point to a dissociation between the neuroanatomical correlates for NLMT and RCFT. Involvement of the right temporal lobe, namely the hippocampus was only observed for the NLMT,

which seems thus to work as a neuropsychological marker for right-temporal lobe functioning.

P161

### Patients with Amyotrophic Lateral Sclerosis and Cognitive Deficits Are Impaired in Recognising Negative Facial Emotions

A. Meyer <sup>1</sup>, A. Semenkova <sup>2</sup>, C. Gerber <sup>2</sup>, D. Lulee <sup>3</sup>, N. Braun <sup>4</sup>, K. Schweikert <sup>5</sup>, M. Weber <sup>4</sup>, J. Wendebourg <sup>6</sup>, R. Schlaeger <sup>6</sup>, R. Kressig <sup>7</sup>, O. Piguet <sup>8</sup> and M. Sollberger <sup>9</sup>

<sup>1</sup> Memory Clinic, University Department of Geriatric Medicine FELIX PLATTER, Switzerland

<sup>2</sup> Memory Clinic, University Department of Geriatric Medicine FELIX PLATTER/Faculty of Psychology, University of Basel, Switzerland

<sup>3</sup> Department of Neurology, Ulm University Medical Center, Ulm, Germany

<sup>4</sup> Kantonsspital St. Gallen Muskelzentrum/ALS Clinic, St. Gallen, Switzerland

<sup>5</sup> REHAB Basel, Basel, Switzerland/Department of Neurology, University Hospital Basel and University of Basel, Switzerland

<sup>6</sup> Department of Neurology, University Hospital Basel and University of Basel, Switzerland

<sup>7</sup> University Department of Geriatric Medicine FELIX PLATTER, Switzerland

<sup>8</sup> School of Psychology and Brain and Mind Centre, The University of Sydney, Australia

<sup>9</sup> Memory Clinic, University Department of Geriatric Medicine FELIX PLATTER/Department of Neurology, University Hospital Basel and University of Basel, Switzerland

**Aims:** Evidence for the presence of emotion recognition disturbance in amyotrophic lateral sclerosis (ALS) is ambiguous. Likely explanations for this variability are heterogeneity of clinical symptomatology with regards to cognition, behaviour and affect, as well as heterogeneity of instruments used to assess emotion recognition. Here, we focused on ALS patients without and with cognitive disorders. These patients were tested with the Facial Emotion Intensity Rating Task—Congruent and Incongruent (FEIRT-CIC), a recently developed sensitive and short test of facial emotion recognition. We aimed to determine whether ALS patients present difficulties in discriminating among the four basic negative facial emotions (i.e., anger, disgust, fear and sadness).

**Methods:** We compared performance on negative facial emotion discrimination between 37 ALS patients [25 without cognitive deficits (pure ALS) and 12 with cognitive deficits (ALSci) according to the Strong et al. (2017) diagnostic criteria] and 37 healthy controls (HC), matched for age, sex and education. Scores of a control task (gender discrimination task) and the FEIRT-CIC were compared across groups using the Wilcoxon-Mann-Whitney-test and Receiver Operating Characteristic analyses.

**Results:** Overall, ALS patients were not impaired in discriminating between gender presented as facial features. They were, however, impaired in discriminating negative emotions overall compared with HC ( $p = 0.05$ ). ALS subgroup analyses revealed the ALSci group to be impaired on negative emotion discrimination ( $p = 0.002$ ) with an AUC of 0.83 (95% CI 0.67–0.99). This deficit was of similar severity for the four negative emotions. In contrast, pure ALS patients showed no impairment in emotion discrimination.

**Conclusions:** We showed that the capacity in negative emotion discrimination in ALS patients varies depending on whether a cognitive impairment is present or not. As a next step, we will analyse whether ALS subgroups with behavioural disorders are more impaired in negative emotion discrimination than the ALSci subgroup.

P162

### Delayed Episodic Memory Recall after One Week Is Predicted by Learning and Executive Functions in Pediatric Epilepsy Patients

M. Studer <sup>1</sup>, S. Schmitt <sup>2</sup>, K. Lidzba <sup>2</sup> and S. Bigi <sup>1</sup>

<sup>1</sup> University Hospital of Neurology, Inselspital Bern, Switzerland

<sup>2</sup> University Children's Hospital, Division of Child Neurology, Development & Rehabilitation, Inselspital Bern, Switzerland

**Objective:** Recent studies suggest that although children with epilepsy may show normal learning and memory performance, accelerated long-term forgetting (ALF) may become evident over time. Our study examined associations between delayed episodic memory performance (recall 1-week after learning) and executive functions.

**Participants and Methods:** A consecutive sample of children with epilepsy without morphologic or metabolic brain abnormalities ( $n = 20$ , mean age: 11.70 years) was compared to an IQ-matched healthy control group ( $n = 20$ , mean age: 11.55 years). We also assessed parents' and children's rating of forgetting in everyday life and explored its association with delayed episodic memory recall.

**Results:** Similar to results from recent studies of patients with temporal lobe epilepsy or genetic generalized epilepsy, our pediatric epilepsy patients showed a significantly reduced 1-week recall, although verbal learning, 30-min recall, and recognition was comparable to a matched control group. Additionally, delayed recall in patients was moderately associated with their subjective rating of forgetting, as well as executive functions (letter fluency, working memory and switching) and divided attention. Furthermore, verbal learning and executive functions predicted 1-week recall in patients, but not in healthy controls.

**Conclusions:** Accelerated long-term forgetting occur in pediatric epilepsy and is associated with executive functions, supporting the idea that reduced delayed memory recall after time illustrates a retrieval impairment. Given the clinical relevance of long-term memory, age-appropriate standard norms for free memory recall after 1 week are desirable.

P163

### The MASC: A Valid Ecological Tool for the Assessment of Theory of Mind in Brain-Injured Patients?

M. Pittet <sup>1</sup>, M. Picard <sup>2</sup>, A. Piolet <sup>2</sup>, A. Sokolov <sup>1</sup> and P. d'Honinckthun <sup>1</sup>

<sup>1</sup> CHUV Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland

<sup>2</sup> Université de Neuchâtel, Switzerland

**Aims:** The ability to infer someone else's thoughts, feelings, and intentions (i.e., the Theory of Mind; ToM) is essential for understanding and efficiently navigating the social world. ToM impairments may compromise professional and social reintegration, yet are typically underestimated in patients with acquired brain damage. Therefore, sensitive and ecological tools are of utmost importance for the neuropsychological assessment of social cognition in brain-injured patients.

A systematic review from our group [1] identified the Movie for the Assessment of Social Cognition (MASC; [2]) as a promising tool with good ecological validity as well as strong psychometric properties in psychiatric populations. The purpose of the present study is to validate this test in patients with acquired brain injury.

**Methods:** Participants: 15 brain-injured patients (following a stroke or a traumatic brain injury, > 3 months post-stroke/traumatic brain injury) presenting with a social cognition deficit in everyday life (OSCARS, Healey et al., 2015), 15 age/sex/education-matched controls.

**Procedure:** Both groups underwent a comprehensive socio-cognitive assessment (9 tasks including the MASC, and 3 questionnaires). We then computed the MASC psychometric properties.

**Preliminary results:** MASC total scores reliably discriminated brain-injured patients from controls ( $p < 0.001$ ). The error pattern differed between patients and controls ( $p < 0.05$ ): patients were significantly more prone to hypomentalize ( $p < 0.001$ ) or to show an absence

of mentalization ( $p < 0.05$ ). Furthermore, the MASC showed a satisfactory internal consistency ( $\alpha = 0.69$ ), test-retest reliability (ICC in patients = 0.87), and at an optimal cutoff at 31 points out of 45, a very good sensitivity/specificity (AUC = 0.88). Finally, MASC total scores as well as affective and cognitive ToM subscales scores significantly correlated with other socio-cognitive tasks.

**Conclusions:** This study demonstrated the sound psychometric properties of the MASC in brain-injured patients. These results set the stage for ecological neuropsychological assessment and rehabilitation of social cognition in patients with acquired brain injury, but also other neurological conditions such as multiple sclerosis, epilepsy, brain tumors or neurodegeneration.

*P164-YouClin*

### **Glial Cells Internalize Increased Amounts of Synaptic Elements in Human Brains of Demented Compared to Resilient Individuals Who Harbour Equivalent Burdens of Amyloid and Tau Deposits**

**R. Taddei**

Massachusetts General Hospital and Harvard Medical School, USA

**Aims:** Synaptic loss is the strongest predictor of cognitive decline in Alzheimer's disease (AD). Yet, presence and burden of amyloid and tau pathologies alone are insufficient to account for the full extent of synapse derangement observed in demented AD brains. We recently showed that increased proinflammatory and decreased homeostatic glial responses are present in the visual cortex of demented but not resilient human AD brains at Braak III-IV stages of tau pathology (1). Moreover, emerging evidence suggests that microglia take up excessive amounts of synapses in human AD brains (2,3), and in vitro models have shown that glial cells are capable of engulfing synapses (4). Yet, human brain derived evidence of aberrant glial-mediated synapse elimination and the underlying contributors remain widely unexplored.

**Methods:** We studied human brains of demented and resilient individuals at intermediate (Braak III-IV) stages of tau pathology that harboured similar burdens of amyloid and tau deposits, and healthy controls without AD neuropathology. We evaluated the visual cortex, a Braak stage VI region, that showed no neurofibrillary tau (NFT) deposits in these brains. We applied expansion microscopy, a novel technique that allows synaptic resolution, and Imaris Software analyses to quantify synaptic densities and evaluate spatial relationships with glial cells in 3D.

**Results:** Our data show that demented brains display significantly lower pre-, post-, as well as colocalized synaptic puncta, and higher proportions of microglial and astrocyte internalized synaptic elements in the visual cortex compared to resilient and control brains.

**Conclusions:** These preliminary results suggest that synaptic density loss precedes NFT deposition in demented human AD brains, serving as a better predictor of cognitive decline than amyloid and tau deposits. Moreover, synapses are excessively internalized by a subset of glial cells in demented compared to resilient and control brains, and this is not only accomplished by microglia but also by a subset of astrocytes. These novel findings favour a model in which glial mediated synapse elimination occurs ahead of NFT formation and predicts cognitive impairment in AD. Our findings could have potential implications for development of novel treatment avenues aimed at preventing cognitive decline in early phases of the disease.

YC-001

## Oral Anticoagulants in the Oldest Old with Recent Stroke and Atrial Fibrillation

A Polymeris <sup>1</sup> and S Engelter <sup>2</sup>

<sup>1</sup> Universitätsspital Basel, Switzerland

<sup>2</sup> University Hospital Basel and University of Basel, Basel, Switzerland

**Objective:** To investigate the safety and effectiveness of direct oral anticoagulants (DOAC) versus vitamin K antagonists (VKA) after recent stroke in patients with atrial fibrillation (AF) aged  $\geq 85$  years.

**Methods:** Individual patient data analysis from seven prospective stroke cohorts. We compared DOAC versus VKA treatment among patients with AF and recent stroke ( $<3$  months) aged  $\geq 85$  versus  $<85$  years. Primary outcome was the composite of recurrent stroke, intracranial hemorrhage (ICH) and all-cause death. We used simple, adjusted, and weighted Cox regression to account for confounders. We calculated the net benefit of DOAC versus VKA by balancing stroke reduction against the weighted ICH risk.

**Results:** In total, 5984 of 6267 (95.5%) patients were eligible for analysis. Of those, 1380 (23%) were aged  $\geq 85$  years and 3688 (62%) received a DOAC. During 6874 patient-years follow-up, the impact of anticoagulant type (DOAC versus VKA) on the hazard for the composite outcome did not differ between patients aged  $\geq 85$  (HR  $\geq 85$  y = 0.65, 95%-CI [0.52, 0.81]) and  $<85$  years (HR  $<85$  y = 0.79, 95%-CI [0.66, 0.95]) in simple (pinteraction = 0.129), adjusted (pinteraction = 0.094) or weighted (pinteraction = 0.512) models. Analyses on recurrent stroke, ICH and death separately were consistent with the primary analysis, as were sensitivity analyses using age dichotomized at 90 years and as a continuous variable. DOAC had a similar net clinical benefit in patients aged  $\geq 85$  (+1.73 to +2.66) and  $<85$  years (+1.90 to +3.36 events/100 patient-years for ICH-weights 1.5 to 3.1).

**Interpretation:** The favorable profile of DOAC over VKA in patients with AF and recent stroke was maintained in the oldest old.

YC-002

## Long-Term Outcome and Quality of Life in Patients With Stroke Presenting With Extensive Early Infarction

M. Beyeler <sup>1</sup>, L. Weber <sup>1</sup>, E. Buffle <sup>1</sup>, C. Kurmann <sup>1</sup>, E. Piechowiak <sup>1</sup>, M. Branca <sup>2</sup>, T. Meinel <sup>1</sup>, S. Jung <sup>1</sup>, D. Seiffge <sup>1</sup>, M. Heldner <sup>1</sup>, S. Pilgram-Pastor <sup>1</sup>, T. Dobrocky <sup>1</sup>, P. Mordasini <sup>1</sup>, M. Arnold <sup>1</sup>, J. Gralla <sup>1</sup>, U. Fischer <sup>1</sup> and J. Kaesmacher <sup>1</sup>

<sup>1</sup> Inselspital, Bern University Hospital and University of Bern, Switzerland

<sup>2</sup> CTU Bern, Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

**Background:** The benefit of mechanical thrombectomy in patients with low Alberta Stroke Program Early Computed Tomography Score (ASPECTS) for short-term outcomes is debatable and long-term outcomes remain unknown. This retrospective, monocentric cohort study aimed to assess the association between reperfusion grade and the long-term functional outcome measured with modified Rankin scale as well as the long-term health-related quality of life recorded at the last follow-up in patients according to baseline ASPECTS (0–5 versus 6–10).

**Methods:** Deceased patients were identified from the Swiss population register and follow-up telephone interviews were conducted with all surviving patients with stroke treated with mechanical thrombectomy between 1 January 2010, and 31 December 2018. Favorable outcome was defined as modified Rankin scale 0 to 3, health-related quality of life was assessed using the 3-level version of the EuroQol 5-dimensional questionnaire. The EuroQol 5-dimension utility index was calculated for statistical analyses. The reperfusion grade was core laboratory adjudicated using the expanded treatment in



cerebral ischemia score. Adjusted odds ratios for the association between the reperfusion grade assessed by expanded treatment in cerebral ischemia and outcomes were calculated from multivariable logistic regression.

**Results:** Of the 1114 patients with available long-term follow-up records (median follow-up, 3.67 years), 997 were included in the final analysis. Respectively, patients with low ASPECTS more often had complaints regarding mobility (67.1% versus 42.1%,  $p < 0.001$ ), self-care (53.4% versus 31.2%,  $p < 0.001$ ), and usual activities (65.8% versus 41.4%,  $p < 0.001$ ) than patients with high ASPECTS, whereas reported pain/discomfort (65.7% versus 69.9%,  $p = 0.49$ ) and anxiety/depression (71.2% versus 78.9%,  $p = 0.17$ ) did not differ. In patients with low ASPECTS, increasing reperfusion grade was associated with a higher likelihood of long-term favorable functional outcome (adjusted odds ratio, 1.43, 95% CI, 1.09–1.88 [ $p = 0.01$ ]) and health-related quality of life (adjusted linear correlation coefficient, 0.05, 95% CI, 0.02–0.08) despite early extensive infarction.

**Conclusions:** Despite low baseline ASPECTS, a higher reperfusion grade results in better functional outcomes and may improve health-related quality of life in the long term.

YC-003

### Spinal Cord Gray Matter Atrophy Is Associated with Functional Decline in Post-Polio Syndrome

M. J. Wendebourg <sup>1</sup>, M. Weigel <sup>2</sup>, L. Richter <sup>3</sup>, V. Gocheva <sup>4</sup>, P. Hafner <sup>4</sup>, A. Orsini <sup>4</sup>, V. Crepulja <sup>3</sup>, S. Schmidt <sup>4</sup>, A. Huck <sup>5</sup>, J. Oechtering <sup>1</sup>, M. Blatow <sup>6</sup>, T. Haas <sup>7</sup>, C. Granziera <sup>8</sup>, L. Kappos <sup>9</sup>, P. Cattin <sup>5</sup>, O. Bieri <sup>2</sup>, D. Fischer <sup>4</sup> and R. Schlaeger <sup>1</sup>

<sup>1</sup> Department of Neurology, Department of Clinical Research, University Hospital Basel and University of Basel, Basel, Switzerland

<sup>2</sup> Division of Radiological Physics, Department of Radiology, University Hospital Basel and Department of Biomedical Engineering, University of Basel, Basel, Switzerland

<sup>3</sup> Department of Neurology, University Hospital Basel, Basel, Switzerland

<sup>4</sup> Division of Pediatric Neurology, University of Basel Children's Hospital, Basel, Switzerland

<sup>5</sup> Department of Biomedical Engineering, University of Basel, Basel, Switzerland

<sup>6</sup> Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich, University of Zurich, Zurich, Switzerland

<sup>7</sup> Division of Radiological Physics, Department of Radiology, University Hospital Basel, Basel, Switzerland

<sup>8</sup> Translational Imaging in Neurology (ThINk), Department of Biomedical Engineering, University of Basel, Basel, Switzerland

<sup>9</sup> MS Center and Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel and University of Basel, Basel, Switzerland

**Aims:** Post-polio syndrome (PPS) is defined by progressive and persistent new muscle weakness or fatigability occurring after a stable interval, decades after the initial viral infection of spinal cord (SC) motor neurons. The aims of this study were to determine if patients with PPS show spinal cord gray matter (SCGM) atrophy using rAMIRA magnetic resonance imaging (MRI) (Wiegel & Bieri, 2018, Weigel et al., 2020) and to assess associations between SCGM atrophy, muscle strength and patient-reported functional decline.

**Methods:** Twenty patients diagnosed with PPS (March of Dimes criteria, 2002) and twenty age- and sex-matched healthy controls (HC) underwent 3T axial 2D-rAMIRA MRI at the intervertebral disc levels C2/C3–C6/C7, T9/T10 and the lumbar enlargement level (Tmax) (0.5 × 0.5 mm<sup>2</sup> in-plane resolution). SCGM areas were segmented manually by two independent raters. Muscle strength, self-reported fatigue, depression, and pain measures were assessed.

**Results:** Post-polio syndrome patients showed significantly and preferentially reduced SCGM areas at C2/C3 ( $p = 0.048$ ), C3/C4 ( $p = 0.001$ ), C4/C5 ( $p < 0.001$ ), C5/C6 ( $p = 0.004$ ) and Tmax ( $p = 0.041$ ) compared to HC. In patients with PPS, SCGM areas were significantly associated with muscle strength in corresponding myotomes even after adjustment for

fatigue, pain, and depression: Adjusted for age and sex, SCGM area at C3/C3 explained 56% of neck flexor strength variance ( $p = 0.002$ ), SCGM area at C5/C6 explained 32% of wrist extension strength variance ( $p = 0.032$ ), and SCGM area at Tmax explained 68% of ankle dorsiflexion strength variance ( $p = 0.006$ ). No associations were found with age at or time since infection. Patients reporting PPS-related decline in arm function showed significant cervical SCGM atrophy compared to stable patients adjusted for initial disease severity.

**Conclusions:** Patients with PPS show significant SCGM atrophy that correlates with muscle strength in corresponding myotomes and is associated with PPS-related functional decline. Our findings suggest a secondary neurodegenerative process underlying SCGM atrophy in PPS that is not explained by aging or residua of the initial infection alone. These results need to be confirmed by longitudinal studies. The methodology presented here is promising for the development of novel imaging surrogates for diseases involving SCGM.

YC-004

### Anatomical Phenotyping and Staging of Brain Tumours

K. Akeret, F. Vasella, V. Staartjes, J. Velz, T. Müller, M. Neidert, M. Weller, L. Regli, C. Serra and N. Krayenbühl

University Hospital and University of Zurich, Zurich, Switzerland

Unlike other tumours, the anatomical extent of brain tumours is not objectified and quantified through staging. Staging systems are based on understanding the anatomical sequence of tumour progression and its relationship to histopathological dedifferentiation and survival. The aim of this study was to describe the spatiotemporal phenotype of the most frequent brain tumour entities, to assess the association of anatomical tumour features with survival probability and to develop a staging system for WHO grade 2 and 3 gliomas and glioblastoma.

Anatomical phenotyping was performed on a consecutive cohort of 1000 patients with first diagnosis of a primary or secondary brain tumour. Tumour probability in different topographic, phylogenetic and ontogenetic parcellation units was assessed on preoperative MRI through normalization of the relative tumour prevalence to the relative volume of the respective structure. We analysed the spatiotemporal tumour dynamics by cross-referencing preoperative against preceding and subsequent MRIs of the respective patient. The association between anatomical phenotype and outcome defined prognostically critical anatomical tumour features at diagnosis. Based on a hypothesized sequence of anatomical tumour progression, we developed a three-level staging system for WHO grade 2 and 3 gliomas and glioblastoma. This staging system was validated internally in the original cohort and externally in an independent cohort of 300 consecutive patients.

While primary CNS lymphoma showed highest probability along white matter tracts, metastases enriched along terminal arterial flow areas. Neuroepithelial tumours mapped along all sectors of the ventriculocortical axis, while adjacent units were spared, consistent with a transpallial behaviour within phylo-ontogenetic radial units. Their topographic pattern correlated with morphogenetic processes of convergence and divergence of radial units during phylo- and ontogenesis. While a ventriculofugal growth dominated in neuroepithelial tumours, a gradual deviation from this neuroepithelial spatiotemporal behaviour was found with progressive histopathological dedifferentiation. The proposed three-level staging system for WHO grade 2 and 3 gliomas and glioblastoma correlated with the degree of histological dedifferentiation and proved accurate in terms of survival upon both internal and external validation.

YC-005

## On the Association between the Choroid Plexus Volume and Disease Characteristics in Multiple Sclerosis

J. Müller<sup>1</sup>, S. Reimann<sup>1</sup>, T. Sinnecker<sup>1</sup>, M. J. Wendebourg<sup>1</sup>, R. Schläger<sup>1</sup>, C. Tsagkas<sup>1</sup>, K. Parmar<sup>2</sup>, A. Pröbstel<sup>1</sup>, M. Amann<sup>3</sup>, J. Würfel<sup>3</sup>, N. Hadjikhani<sup>4</sup>, T. Lincke<sup>5</sup>, M. Barakovic<sup>6</sup>, A. Cagol<sup>6</sup>, L. Melie-Garcia<sup>6</sup>, S. Meier<sup>1</sup>, A. Maceski<sup>1</sup>, E. Willemse<sup>1</sup>, D. Leppert<sup>1</sup>, S. Schädelin<sup>7</sup>, P. Benkert<sup>7</sup>, C. Jud<sup>8</sup>, P. Cattin<sup>8</sup>, J. Kuhle<sup>1</sup>, T. Derfuss<sup>1</sup>, L. Kappos<sup>1</sup>, C. Granziera<sup>1</sup> and Ö. Yaldizli<sup>1</sup>

<sup>1</sup> Neurologic Clinic and Polyclinic, MS Centre and Research Centre for Clinical Neuroimmunology and Neuroscience Basel, Switzerland

<sup>2</sup> Reha Rheinfelden, Switzerland

<sup>3</sup> Medical Imaging Analysis Center AG, Switzerland

<sup>4</sup> Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Harvard Medical School, USA

<sup>5</sup> University Hospital Basel and University of Basel, Section of Neuroradiology, Clinic for Radiology & Nuclear Medicine, Switzerland

<sup>6</sup> Translational Imaging in Neurology Basel, Department of Biomedical Engineering, University Basel, Switzerland

<sup>7</sup> University Basel, Department of Clinical Research, Clinical Trial Unit, Switzerland

<sup>8</sup> University of Basel, Department of Biomedical Engineering, Switzerland

**Introduction:** The choroid plexus (CP) has been proposed as a modulator of MS-related inflammation. We previously showed that the CP is larger in MS than healthy controls (HCs) and neuromyelitis optica spectrum disease. However, data about the correlations between CP volume (CPV) and MS disease characteristics are scarce.

**Aim:** To investigate the associations between CPV and disease characteristics in RRMS.

**Methods:** Cross-sectional, retrospective study. We included 109 RRMS patients from the Swiss MS cohort study (Basel center; mean age  $46.9 \pm 10.9$  years; 69% female; mean disease duration  $16 \pm 9$  years; proportion of patients with a relapse within the previous year = 11%; median EDSS 2.5 [IQR = 2]) and 118 HCs (mean age  $44.3 \pm 13.4$  years; 65% female). The CP of the lateral ventricles was segmented fully automatically using an in-house deep learning algorithm on non-contrast T1-weighted(w) MRI. Serum neurofilament light chain (sNfL) was measured using the latest HDX platform from Quanterix®. We compared the sNfL values of the patients with a large normative database ( $n > 10,000$  HCs) and calculated z-scores using a generalized additive model for location, scale and shape (Benkert et al. Lancet 2022). Associations between CPV and disease characteristics were investigated using multivariable linear regression models.

**Results:** CP was larger in RRMS than HCs ( $B = 221$ , 95% CI: 111–331,  $\text{Beta} = 0.25$ ,  $p < 0.001$ , adjusted for age, gender and TIV). In HCs, CPV correlated with the lateral ventricle volume (LVV;  $B = 0.016$ , 95% CI: 0.009–0.024,  $\text{Beta} = 0.39$ ,  $p < 0.001$ , adjusted for age, gender and TIV). In RRMS, there was no association between CPV and disease duration, log(EDSS), relapses in the last year, sNfL z-score or disease-modifying treatment. However, CPV was associated with volume ( $B = 10.6$ , 95% CI: 5.4–15.9,  $\text{Beta} = 0.35$ ,  $p < 0.001$ ) and number ( $B = 5.8$ , 95% CI: 2.5–9.1,  $\text{Beta} = 0.30$ ,  $p = 0.001$ ) of the T2w lesions adjusted for age, gender and TIV. Every mL increase of T2w lesion volume was associated with a 11  $\mu\text{L}$  larger CP. In a multivariable analysis including age, gender, TIV, disease duration, relapse in the last 12 months (yes/no), log(EDSS), disease-modifying treatment, sNfL z-score, T2w lesion volume and LVV, the LVV was the only parameter that was associated with the CPV in RRMS ( $B = 0.014$ , 95% CI: 0.009–0.02,  $\text{Beta} = 0.62$ ,  $p < 0.001$ ).

**Conclusions:** LVV as a surrogate of brain atrophy is more closely associated to the CPV than the T2w lesion burden in RRMS.

**Funding:** J. Müller reports no competing interests. S. Reimann reports no competing interests. T. Sinnecker is parttime employee of the Medical Image Analysis Center Basel. MJ. Wendebourg reports no competing interests. R. Schlaeger reports no competing interests. Ch. Tsagkas reports no competing interests. K. Parmar reports no competing interest. AK. Pröbstel received speaker fees, travel support, and/or served on advisory boards of Novartis Pharma and Roche; she received

research support from Biogen, the Swiss National Research Foundation, the National Multiple Sclerosis Society, the European Research Council, University of Basel, the Propatient Foundation, and the Goldschmidt-Jacobson Foundation. M. Amann reports no competing interests. J. Wuerfel is employee of MIAC AG; he served for advisory boards for Biogen, Idorsia, Novartis, Roche, and Sanofi; he is or was supported by the EU (Horizon2020), the German Ministries for Economy and Science and Education. N. Hadjikhani reports no competing interest. T. Lincke reports no competing interest. M. Barakovic reports no competing interest. A. Cagol reports no competing interest. L. Melie-Garcia reports no competing interest. S. Meier reports no competing interest. A. Maceski reports no competing interest. E. Willemse reports no competing interest. D. Leppert is Chief Medical Officer of GeNeuro. S. Schaedelin reports no competing interest. J. Kuhle received speaker fees, research support, travel support, and/or served on advisory boards byECTRIMS, Swiss MS Society, Swiss National Research Foundation [320030\_160221], University of Basel, Bayer, Biogen, Genzyme, Merck, Novartis, Protagen AG, Roche, and Teva. P. Benkert reports no competing interest. C. Jud reports no competing interest. P. Cattin reports no competing interest. J. Kuhle received speaker fees, research support, travel support, and/or served on advisory boards byECTRIMS, Swiss MS Society, Swiss National Research Foundation [320030\_160221], University of Basel, Bayer, Biogen, Genzyme, Merck, Novartis, Protagen AG, Roche, and Teva. T. Derfuss received speaker fees, travel support, and/or served on advisory boards or steering committees of Novartis Pharma, Merck, Biogen, GeNeuro, Mitsubishi Pharma, MedDay, Roche, Celgene, Alexion, Actelion, and Genzyme; he received research support from Biogen, Novartis, Roche, Alexion, the Swiss National Research Foundation, University of Basel, and the Swiss MS Society. L. Kappos' institution (University Hospital Basel) received and used exclusively for research support: steering committee, advisory board, and consultancy fees (Actelion, Bayer HealthCare, Biogen, BMS, Genzyme, Janssen, Merck, Novartis, Roche, Sanofi, Santhera, and TG Therapeutics); speaker fees (Bayer HealthCare, Biogen, Merck, Novartis, Roche, and Sanofi); support of educational activities (Allergan, Bayer HealthCare, Biogen, CSL Behring, Desitin, Genzyme, Merck, Novartis, Roche, Pfizer, Sanofi, Shire, and Teva); license fees for Neurostatus products; and grants (Bayer HealthCare, Biogen, European Union, InnoSwiss, Merck, Novartis, Roche, Swiss MS Society, and Swiss National Research Foundation). C. Granziera's institution, the University Hospital Basel (USB), has received the following fees, which were used exclusively for research support: (1) advisory board and consultancy fees from Actelion, Novartis, Genzyme-Sanofi, and F. Hoffmann-La Roche Ltd; (2) speaker fees from Biogen and Genzyme-Sanofi; and (3) collaborative research funds by F. Hoffmann-La Roche Ltd. Ö. Yaldizli received grants fromECTRIMS/MAGNIMS, University of Basel, Pro Patient Stiftung, University Hospital Basel, Free Academic Society Basel, and the Swiss Multiple Sclerosis Society and advisory board fees from Roche, Sanofi Genzyme, Biogen, Almirall, and Novartis.

**Conflicts of Interest:** The authors declare no conflict of interest.