CLINICAL and TRANSLATIONAL NEUROSCIENCE

Clinical & Translational Neuroscience
2018, Vol. 2(Supplement) 1S–34S

DOI: 10.1177/2514183X18802121
journals.sagepub.com/home/ctn
SAGE

Annual Congress 2018 of the Swiss Neurological Society SNS

Abstract book

Jahrestagung 2018
Schweizerische Neurologische Gesellschaft
2m2c Montreux Music & Convention Centre, Schweiz
sng2018.congress-imk.ch

Réunion annuelle 2018
Société Suisse de Neurologie
2m2c Montreux Music & Convention Centre, Suisse
sng2018.congress-imk.ch

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GemSession (SAYN)
Donnerstag | Jeudi 27.09.2018, 15:30-16:30

M01*
Modeling synapses and synaptic neuropsychiatric disorders using human brain organoids

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Human cerebral organoids currently represent a state-of-the-art human-brain model to study human neuropsychiatric and neurodevelopmental disorders for which mouse models show major limitations. Synaptic connections in the human brain define neural circuits, and their deficits cause neuropsychiatric disorders. Harnessing the full power of the cerebral organoid model requires the ability to visualize and analyze synapses in the cerebral organoids. Here, we report an optimized method to develop human cerebral organoids, and investigate the possibility of modeling synapses in the organoids. We give evidence for synaptogenesis in the cerebral organoids. We show that optimal cerebral organoids express mature-neuron markers, including synaptic proteins and neurotransmitter receptors and transporters. Moreover, we describe various assays to visualize and analyze synapses in the organoids. These results indicate that cerebral organoids can be used to model human brain synaptopathies and understand the moleweekly [Phase II]). Patients completing controlled bases for neuropsychiatric disorders.

M02*
Deconstructing frontal gait in normal pressure hydrocephalus

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Aims:
Gait disturbance in idiopathic normal pressure hydrocephalus (iNPH) is classically described as slow, magnetic and wide-based, also known as frontal gait. However, the clinical gait abnormalities found in iNPH are unspecific and also found in alternate neurological conditions mimicking iNPH (also called iNPH mimics), such as vascular dementia or dementia with Lewy bodies. This study aims to compare the prevalence of clinical gait abnormalities between iNPH and iNPH mimics.

Methods:
A total of 140 patients with a suspicion of iNPH (76.3 $\pm$ 6.8 yo; 30.7% female) were included in this retrospective study. Eighty patients (57.1%) fulfilled the NPH consensus guidelines criteria; and the remaining sixty patients were classified as iNPH mimics (23 neurodegenerative condition, 13 multifactorial conditions, 10 vascular dementia, 7 toxic cause, and 7 mixed dementia). The clinical gait characteristics were rated by two independent clinicians blinded for the diagnosis (EM and GA, kappa, 0.73). Clinical gait characteristics included four categories: frontal gait (short step, wide-based, reduced step height), parkinsonian gait (short and/or shuffling steps, flexed posture, reduced arm swing and narrow base), other clinical gait abnormalities and normal gait.

Results:
Clinical characteristics were similar between iNPH and iNPH mimics. Frontal gait was not the most prevalent clinical gait abnormalities among both groups (only a quarter of both groups). The prevalence of frontal gait was similar between iNPH and iNPH mimics; while parkinsonian gait was more prevalent among the iNPH mimics (32% versus 15%; p-value: 0.032). This association between parkinsonian gait and iNPH mimics remains significant after adjusting for age, gender, comorbidities and white matter changes (OR: 0.416; 95% CI: [0.18 – 0.98]; p value: 0.044).

Conclusion:
Frontal gait is not the most prevalent clinical gait abnormalities among patients with suspicion of iNPH and does not help to identify iNPH from iNPH mimics. Parkinsonian gait differentiates the mimics from the iNPH patients and may represent a red flag for an alternate condition when assessing a patient with suspicion of iNPH.

M03*
The caudal vermis and the dentate nucleus are critical structures for determining the directional asymmetry in gaze-evoked nystagmus in unilateral cerebellar lesions

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Aims:
Stabilizing the eyes in space when looking at a target is provided by a brainstem/cerebellar gaze- holding network. While lesion studies in non-human primates pointed to a key role of the flocculus/paraflocculus complex in gaze holding, observations in humans indicated an involvement of the caudal vermis, the biventer lobule and the inferior semilunar lobule. Previous research suggested that acute lateralized cerebellar lesions preferentially lead to gaze-evoked nystagmus (GEN) on ipsilesional gaze. We aimed to further characterize GEN-asymmetry in unilateral cerebellar stroke and hypothesized that the direction of gaze-holding impairment depends on the location of the lateralized lesions.

Methods:
Nine patients (aged 31-62y, 2 females) with acute/subacute (less than 10d old) MRI-confirmed unilateral cerebellar

stroke were included. Horizontal gaze holding was quantified (range= ±40° gaze) while a flashing target was slowly (0.5°/s) moving. Asymmetry in eye-drift velocity was calculated and compared to the different patterns in cerebellar lesions.

Results:
Individual peak eye drift velocities ranged from 3.9°/s to 17.4°/s and occurred at the most eccentric eye positions (30-40° of lateral gaze). We found significantly asymmetric GEN in 7/9 patients, which increased progressively with increasing eccentricity of eye position, indicating a non-linear behavior similar to the one observed in patients with degenerative cerebellar disease. Those patients with MRI- confirmed involvement of the caudal vermis and the dentate nucleus all presented with predominantly ipsilesional GEN (n=4), while in those with lesions restricted to the cerebellar hemisphere GEN was stronger on contralesional gaze in three out of four patients.

Conclusion:
Involvement of the caudal vermis (uvula, nodulus) and the dentate nucleus is critical for determining the directional asymmetry in GEN in unilateral cerebellar lesions, while the flocculus played a minor role only in human gaze-holding in our study. Specifically, the asymmetry in GEN in relation to the side of the lesion predicted which cerebellar structures have been damaged.

M04*
CT imaging markers of cerebral amyloid angiopathy, APOE genotype and recurrent ICH risk – the Edinburgh CAA criteria

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Background:
We analysed the rate of recurrent intracerebral haemorrhage (ICH) applying the Edinburgh criteria for cerebral amyloid angiopathy (CAA).

Methods:
In a prospective ICH cohort study, we analysed CT scans for presence of subarachnoid haemorrhage (SAH) and "finger-like projections" (FLP). We used blood samples to determine APOE genotype. Patients were followed up for at least 6 months for recurrent ICH. We calculated annualized rate of recurrent ICH (=total of observed ICH/patient-years of follow-up) and assessed association with recurrent ICH using multivariate (adjusted for age and sex) cox regression models. We calculated hazard ratios (HR) and corresponding 95% confidence intervals (95%CI).

Results:
The final cohort contained 339 patients with lobar ICH (median age 77 years, IQR 70-83; median ICH- volume 14.8 mL IQR 5.3-31.0 mL). SAH was present in 135 patients (39.8%), FLP in 80 (23.6%) and 104 (30.7%) patients had at least one APOE e4 allele. During a total follow-up period of 490 patient years, 22 patients had recurrent ICH (4.5%/year, CI95% 2.8-6.7%). Patients fulling the full Edinburgh criteria (22 patients/6.5%), had the highest rate of recurrent ICH (11.2%/year, 95%CI 3.1-26.3%) and were over 3 times more likely to have a recurrent ICH than those who did not fulfil the full criteria (HR 3.3, 95%CI 1.1-9.9, p=0.034). Patient with CT only Edinburgh criteria (n=52 patients/15.3%) had similar rates of recurrent ICH as the full criteria (12.2%/year, 95%CI 5.4-22.6%, HR 3.4, 95%CI 1.4-8.2, p=0.006).

Conclusion:
The Edinburgh criteria identify patients at high risk of recurrent ICH. If genetic testing is unavailable, using the CT only criteria is also suitable.

M05*
Direct oral anticoagulants versus Vitamin K antagonists after a recent ischaemic stroke or TIA– a pooled individual patient data analysis

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Background:
We compared clinical outcomes after treatment with direct oral anticoagulants (DOAC) and Vitamin-K antagonists

(VKA) in patients with atrial fibrillation (AF) with a recent ischaemic stroke or TIA.

Methods:
We conducted an individual patient data analysis of 7 prospective cohort studies. We included patients with AF and a recent ischaemic stroke or TIA (< 3 months before starting oral anticoagulation) and a minimum follow-up of 3 month. We analyzed the association between type of anticoagulation (DOAC vs. VKA) with the composite primary endpoint (recurrent ischaemic stroke [AIS], intracerebral haemorrhage [ICH], or mortality) using mixed effects Cox proportional hazards regression models; we calculated adjusted hazard ratios (HRadj) with 95% confidence intervals (95% CI).

Findings:
We included 4912 patients (median age 78 years [IQR71-84]; 2331 [47.5%] women) of whom 4739 (96.5%) had ischaemic stroke as the index event (median NIHSS-at-onset 5 [IQR2-12]); 2256 (45.9%) patients received VKA and 2656 (54.1%) DOAC. The median time from index event to starting oral anticoagulation was 5 days (IQR 2-14) for VKA and 5 days (IQR 2-11) for DOAC (p = 0.53). There were 262 AIS (4.4%/year), 71 ICH (1.2%/year) and 439 deaths (7.4%/year) during the total follow-up of 5970 patient-years. Compared to VKA, DOAC treatment was associated with reduced risks of the composite endpoint (HRadj 0.81, 95%CI 0.66-0.98, p = 0.03), ICH (HRadj 0.33, 95%CI 0.16-0.70, p < 0.01) and mortality (HRadj 0.73, 95%CI 0.57-0.93, p = 0.01); for the risk of recurrent AIS, we found no difference in risk (HRadj 1.02, 95%CI 0.74 - 1.40, p = 0.91).

Conclusion:
DOAC treatment initiated after a median of 5 days after cerebral ischaemia related to AF was associated with reduced risk of poor outcome compared to VKA, mainly due to lower risks of ICH and mortality.

M06*
Effectiveness of fingolimod as first-line and second-line treatment for RRMS patients in Switzerland

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Aim:
Fingolimod is indicated as first-line treatment of relapsing-remitting multiple scleroses (RRMS) in Switzerland.1 In the following analysis, we utilized real world evidence data to compare effectiveness of fingolimod in previously naïve and pre-treated patients.

Methods:
The study is based on a sub-analysis of a cross-sectional, retrospective study conducted in 19 centers in Switzerland. Included RRMS patients received fingolimod for a minimum of 7 and up to 58 months.2 Demographic as well as clinical data was collected. Effectiveness of treatment was evaluated by freedom from relapses and Gd+-enhancing lesions. Analyses were performed using Wilcoxon- and paired t-tests (SAS® package, version 9.2 or higher).

Results:
From 274 analyzed RRMS patients, 79 (28.7%) patients were treatment-naïve and the remaining 196 (71.3%) patients were switched to fingolimod from another therapy.

Seventy-six (97.4%) treatment-naïve and 120 (61.2%) pre-treated patients experienced at least one relapse in the 2 years preceding fingolimod initiation. After a mean (SD) fingolimod treatment duration of 32 (11.8) months, 58 (74.4%) treatment naïve and 155 (79.1%) pre-treated patients remained free from relapses. Within pre-treated individuals, the proportion of relapse-free patients was increased under fingolimod as compared to the 2 years preceding treatment switch: 33/42 (78.6%) vs 25/42 (59.5%) in those switching from natalizumab, 119/150 (79.3%) vs 48/150 (32%) in those switching from IFNβ or glatiramer acetate (p < 0.001 for both comparisons). The proportion of patients experiencing more than 1 relapse changed from 50% to 3.8% and from 22.4% to 7.1% when comparing before vs under fingolimod, in previously naïve and pretreated patients, respectively (p < 0.001 for both comparisons). Similarly, the proportion of patients remaining free from Gd+ lesions before vs after fingolimod start increased from 41.6% to 87.9% in naïve, and from 78.7% to 91.7% in pre-treated patients (p < 0.001 for both comparisons).

Conclusion:
In this Swiss cohort, fingolimod demonstrated a good efficacy profile in terms of both clinical relapses and MRI

activity in naïve as well as pre-treated patients, supporting its use for both indications.

Freie Mitteilungen II | Communications libres II
Freitag | Vendredi 28.09.2018, 08:15-09:45

M07
Characterising in vivo tau-related white matter deficits in Alzheimer's disease

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Aims:
To examine the relationship between [18F]-AV1451 binding (tau) and diffusion tensor imaging (DTI) of white matter changes in Alzheimer's disease (AD).

Methods:
people with clinically probable AD and 14 people with mild cognitive impairment (MCI, with amyloid positive PET imaging) and 24 similarly-aged healthy controls underwent 3T DTI to estimate parameters of Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD), and Radial Diffusivity (RD). A subset of 24 people with AD/MCI also underwent [18F]-AV1451 PET imaging, with PetSurfer quantification of cortical binding potential. Tract Based Spatial Statistics (TBSS) with non-parametric permutations testing were performed to compare DTI parameters in AD/MCI against healthy controls and identify associations of [18F]-AV1451 binding with DTI parameters.

Results:
TBSS confirmed widespread changes in FA, MD and RD parameters in the AD/MCI group compared to controls while adjusting for age and gender (Threshold Free Cluster Enhancement, TFCE $p < 0.05$). Among people with AD/MCI, the cortical [18F]-AV1451 binding estimates of the Tau burden correlated with widespread reductions in FA and increased RD (TFCE $p < 0.05$).

Conclusion:
The use of multimodal brain imaging provides in vivo evidence to link tau pathology to changes in white matter. Our findings corroborated previous evidence from histopathology and CSF studies to implicate cortical neurodegeneration as a potential pathophysiological mechanism underpinning white matter pathologies in AD.

M08
Ischaemic stroke despite oral anticoagulant therapy in patients with AF – what is the risk of recurrent events and how to prevent further events?

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Background/Aim:
We investigated whether patients with atrial fibrillation (AF) having a stroke despite oral anticoagulant therapy a) are at increased risk for further events and b) changing the type of anticoagulant is associated with a decreased risk of further events.

Methods:
We conducted an individual patient data analysis of 7 prospective cohort studies recruiting patients with AF and an index event (ischaemic stroke or TIA). We compared patients taking oral anticoagulants (Vitamin K antagonists [VKA] or direct oral anticoagulants [DOAC]) prior to index event (OACprior) with those without prior anticoagulation (OACnaive). We further compared those who changed the type (i.e. VKA or DOAC) of anticoagulation (OACchanged) with those who continued the same anticoagulation after the event (OACunchanged). We followed-up patients for at least 90 days for recurrent ischaemic stroke (AIS), intracerebral haemorrhage (ICH) or mortality. Time-to-endpoint was analysed using multivariate cox proportional hazard regression models with frailty term for study and calculating hazard ratios (HR) with corresponding 95% confidence intervals.

Results:
We included 5413 patients in this study (median age 78years [IQR 71-84years], 5136 [96.7%] had ischaemic stroke as index event, median NIHSS-on-admission 6 [IQR 2-12]). During follow-up of 6128 patient years, 289 patients had AIS (4.7%/year, 95%CI 4.2-5.3%), 90 patients had ICH (1.5%/year, 95%CI 1.2 -1.8%) and 624 patient died (10.2%/year, 95%CI 9.4-11.0%). priorOAC (n=1195) was associated with an increased risk of recurrent AIS (HR 1.6 95%CI 1.1-2.1, p=0.006) compared to OACnaive (n=4119). OACchanged (n=307) was not associated with decreased risk of recurrent AIS (HR 1.3, 95%CI 0.8-2.2, p=0.326) compared to OACunchanged (n=585).

Conclusion:
Patients having a stroke despite anticoagulation therapy are at increased risk of further events. More research is needed to investigate mechanisms of recurrent stroke and improve secondary prevention in these patients.

M09
MOG-IgG antibodies in autoimmune demyelinating CNS disorders – retrospective analysis of a monocentric patient cohort

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Aims:
The discovery of the pathogenic antibody directed against Aquaporin-4 (AQP4) re-defined neuromyelitis optica spectrum disorders (NMOSD). The antibody directed against myelin- oligodendrocyte-glycoprotein (MOG-IgG) might define another disease entity. An approach to define diagnostic criteria for so-called "MOG encephalomyelitis" (MOG-EM) has recently been published.

Methods:
Clinical and paraclinical data of patients with positive (>1:10) or borderline positive (=1:10, test cut- off) results of serum MOG-IgG, tested in a cell-based assay, were analyzed in a retrospective study.

Results:
We identified 40 patients. Of these, 3 patients did not demonstrate findings compatible with a demyelinating CNS disorder (qualified as unspecific, not included in analyses). For the remaining 37 patients, median age at onset was 28 years (IQR 18.5-40.5). All patients below 18 years at onset (9, 11, 14, 15, 16, 17, 17 years) experienced a first manifestation with a spinal cord or optic nerve syndrome. The female: male ratio was 1.6:1. The last EDSS score was 2.0 (median, IQR 1.5-3.0; max. EDSS 8.0). Classified by EDSS functional systems (FS), onset was monosymptomatic in 18/34, polysymptomatic in 16/34 patients with the majority of patients exhibiting a visual and/or sensory onset (n=13 each), followed by pyramidal symptoms (n=9). In 2 patients with (meningo-) encephalomyelitis, FS classification was not appropriate (multifocal, reduced consciousness, seizures, movement disorder). The first manifestation was an optic nerve or spinal cord syndrome (n=12 each), followed by cerebral and brainstem syndromes (n=6 each) and cerebellar involvement (n=1). All patients were seronegative for AQP4 antibodies. In 4 patients, onset of symptoms was para-/postinfectious, 2 with unknown pathogen after extensive work-up, 1 with VZV and 1 with EHEC, respectively. In the patient with EHEC-associated sepsis and consecutive relapsing bilateral optic neuritis, serum available from the acute phase of infection was retrospectively tested negative for MOG-IgG.

Conclusion:
MOG-EM is not limited to a predominant involvement of optic nerve and spinal cord; brainstem and cerebellar involvement and (atypical) encephalitis can occur. As recently suggested, MOG-IgG testing should thus not be limited to AQP4 antibody negative NMOSD. The para-/postinfectious disease onset of MOG-EM not resembling ADEM has not been described, yet. It may provide hints to the underlying immunological mechanisms.

M10
Cervical Spinal Cord Gray and White Matter Atrophy in Patients with Post-Polio Syndrome

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Aims:
Post-polio syndrome (PPS) is defined as a progressive persistent new muscle weakness or fatigability occurring after a stable interval, years to decades after the initial viral infection of spinal cord (SC) motor neurons (Baj et al. Int J Infect Dis. 2015:35:107). The precise mechanisms underlying PPS are yet to be known. Recent advances in MR sequence development now allow for reliable quantitation of SC gray matter (GM) and white matter (WM) in vivo. The aim of this study was to quantitate SC GM and WM in PPS patients in comparison to healthy age and sex matched control subjects and to correlate GM areas to segmental muscle strength.

Methods:
patients with PPS (mean age 66.5 years [SD 4.53], 12 men) and 20 age and sex-matched healthy controls (HC) were investigated clinically (including quantitative muscle strength assessments of selected target muscles by dynamometer) and at 3T by axial 2D-AMIRA imaging (in plane resolution 0.5x0.5 mm) (Weigel & Bieri. Magn Reson Med. 2018:79:1870) perpendicular to the SC at the intervertebral disc levels C2/C3, C3/C4, C4/C5, C5/C6 and C6/C7. Total cord areas (TCA) were segmented semi-automatically via JIM 7 (www.xinapse.com). SC GM areas

were segmented manually. SC WM areas were calculated by subtracting GM area from TCA.

Results:
Compared to the HC subjects, PPS patients showed significant SC GM atrophy at all levels (C2/C3 p=0.0405, C3/C4 p=0.0002, C4/C5 p < 0.0001, C5/C6 p=0.0006, C6/C7 p=0.0356) and significant SC WM
atrophy at the levels C2/C3 (p=0.0175), C3/C4 (0.0134) and C4/C5 (0.0288). GM area at C2/C3 correlated with neck flexor muscle strength measured by dynamometer (r= 0.64, p=0.0223).

Conclusion:
AMIRA imaging is a sensitive method to quantitate SC GM and WM atrophy in vivo. Cervical SC GM and WM areas were reduced in PPS compared to HC. Spinal cord GM at C2/C3 correlated with muscle strength in the corresponding myotome in PPS. Longitudinal studies are necessary to investigate atrophy over time, its relation to symptom evolution and possible prognostic value. The methodology used here is promising for the development of novel imaging surrogates not only for PPS, but also for other neurodegenerative, genetic or autoimmune mediated diseases of the spinal cord.

M11
Vitamin D Supplementation: A therapeutic strategy to augment steroid treatment of acute Multiple Sclerosis Relapses

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Objective:
Limited efficacy of glucocorticoids (GCs) during acute relapse of multiple sclerosis (MS) leads to increase of MS associated disability in approximately 40% of patients. We investigated the potential of vitamin D (VD) to enhance steroid efficacy for MS relapse therapy.

Methods:
T-cell apoptosis was analysed by FACS. Glucocorticoid receptor (GR) protein was measured using ELISA. MOG35-55 Experimental autoimmune encephalomyelitis (EAE) was performed in wt animals and in those with T-cells deficient for GR-/mTORc1-expression. VD-levels (immunoassay) were analysed in MS patients with stable disease (n=56), relapse responsive (n=30) or resistant to GC treatment (n=24). Gene expression of human T-cells (microarrays, n=112) were correlated with VD-levels.

Results:
In vitro, VD induced the expression of GR protein resulting in a significant increase of Glucocorticoid- induced T-cell apoptosis. VD/GC combination therapy ameliorated EAE disease course more efficiently than respective monotherapies. This effect was dependent on the presence of the GR in T-cells. In the human situation, VD-deficiency was significantly more sever in MS patients during relapse resistant to GC treatment and resulted in a reduced expression of the T-cell GR. The signaling pathway beyond this GR upregulation was via mTORc1 as VD inhibited mTORc1 activity in murine T-cells in vitro. Furthermore, hypovitaminosis D was associated with reduced expression of mTORc1 inhibiting TSC-1 in human T-cells. Finally the upregulation of the GR by VD as well as the functional VD/GC synergism in vitro and in vivo were absent in mice with mTORc1 deficient T-cells and pharmacological inhibition of mTORc1 (everolimus) augmented GC effects in wt animals during EAE even more potent than VD co-administration.

Interpretation:
VD increases therapeutic effects of GCs. The mechanism behind the described synergism is an mTORc1 dependent upregulation of the GR. Our data should stimulate clinical studies investigating the efficacy of a VD/mTOR based approach to treat MS relapses.

M12
Why do patients on anticoagulants bleed in the brain? - Small vessel disease burden in intracerebral haemorrhage associated with oral anticoagulants

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Objectives:
We thought to determine the burden of small vessel disease (SVD) and its association with functional outcome in patients with intracerebral haemorrhage (ICH) associated with the use of oral anticoagulants (OAC, OAC-ICH).

Methods:
In a prospective cohort study of ICH patients with (OAC-ICH) and without (non-OAC ICH) prior use of OAC (Vitamin K antgonists or direct oral anticoagulants), we assessed the association of SVD markers (white matter lesions, lacunes, cortical and deep atrophy, perivascular spaces, cerebral microbleeds and cortical superficial siderosis) and poor functional outcome (defined as modified Rankin Scale score 4-6 at 6 month) using univariate and multivariate logistic regression models with odds ratio (OR) and 95% confidence intervals (95%CI).

Results:
We included 1030 patients (all with CT and 234/22.7% had an additional MRI): 421 (40.9%) with OAC- ICH and 609

(59.1%) with non-OAC ICH. Patients with OAC-ICH were older (median age 79 years, IQR 72-84 years vs. 72 years IQR 62-80 years, $p < 0.001$) and had more often cardiovascular comorbidities (i.e. diabetes mellitus, hypertension, hypercholesterolemia) but there was no difference in ICH-volume (OAC-ICH: 7.2 ml IQR 2.4-20.6 ml vs. non-OAC ICH: 6.9 ml, IQR 2.1-16.0 ml, p=0.22).

Patients with OAC-ICH had more often white matter lesions and atrophy on CT and MRI and perivascular spaces and lobar microbleeds on MRI. The median SVD score was higher in patients with OAC-ICH using both, CT (OR 1.3, 95%CI 1.1 -1.5, p=0.001) and MRI (OR 1.5, 95%CI 1.1-2.1, p=0.010).

However, after adjusting for confounders, we did not find differences in SVD markers or burden between both groups. In multivariate analysis, poor functional outcome was associated with SVD burden on CT (OR 1.5 95%CI 1.1-2.1, p=0.009) but not with OAC-ICH.

Interpretation:
Patients with OAC-ICH have a high burden of SVD which is driven by older age and a higher prevalence of vascular risk factors. SVD burden but not OAC-ICH is associated with poor outcome.

M13
Outcome of patients with large vessel occlusion, mild symptoms, and reperfusion therapies: analysis of the Swiss Stroke Registry, SSR

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Aims:
Efficacy and safety of endovascular treatment (EVT) in patients with acute ischaemic stroke, large vessel occlusion (LVO) and mild symptoms have not been proven. Randomized controlled (RC) EVT trials have mainly excluded patients with NIHSS ≤ 5. We aimed at comparing functional outcome and safety after 90 days in patients with LVO and low NIHSS (≤ 5) undergoing EVT vs intravenous thrombolysis (IVT).

Methods:
We performed a multicentre retrospective analysis of data from the Swiss Stroke Registry. Primary endpoint was favourable functional outcome (modified Rankin Scale [mRS] 0 -1) at 3 months. Secondary outcomes were mRS shift analysis at 3 months, independence (mRS 0-2), survival with high disability (mRS 4-5), mortality and symptomatic intracerebral haemorrhage (sICH). IVT and EVT patients were matched 1:1 by using propensity scores (PS) based on age, sex, baseline NIHSS, pre- stroke mRS, time to treatment, occlusion site and anticoagulation therapy. Differences in outcomes were tested using multivariate logistic and ordinal regression models.

Results:
Out of 11'356 acute stroke patients, 339 met inclusion criteria (n=153 were treated with EVT [n=74 with direct EVT, n=79 with bridging therapy, IVT + EVT] and n=186 were treated with IVT only). After matching by PS, 126 in both groups were available for analyses. A similarly large proportion of EVT and IVT patients reached a favourable outcome at 3 months (57% vs 66% respectively; OR= 0.65, 95% CI= 0.36 -1.17, p=0.15). The proportion of patients reaching independence was slightly lower in EVT than IVT (77% vs 87%; OR= 0.47, 95%CI= 0.22 -1.01, p=0.054). EVT patients also had greater mRS at 3 months by shift analysis (OR= 1.60; 95%CI= 1.02-2.54, p=0.043). This was largely mediated by higher mortality rates among EVT than IVT (10% vs 3%; OR= 3.51, 95% CI= 1.04-11.85, p= 0.043), while the proportion of survived patients with high disability was similarly low (6% vs 3%; OR=2.56, 95%CI=0.68-9.61, p=0.165). sICH were overall relatively rare in two groups (EVT 5% vs IVT 1%, OR= 5.58, 95%CI= 0.57- 54.86, p=0.140. Age was inversely associated with independency (OR= 0.94, 95% CI= 0.91-0.98, p=0.002).

Conclusion:
In acute stroke patients with LVO and mild neurological symptoms, EVT and IVT appear similarly effective in terms of achieving a favourable functional outcome at 3 months, but EVT might be inferior to IVT with regard to mortality and outcome across all levels of disability. Further research is needed.

M14
Buzzing Sympathetic Nerves: A New Test to Enhance Reflex Pupil Dilation in Suspected Horner Syndrome

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Introduction:
Patients with suspected Horner syndrome and equivocal pupil dilation lag and pharmacologic testing might undergo

unnecessary MR imaging. Our purpose was to increase the diagnostic sensitivity of pupillometry by accentuating sympathetic innervation to the iris dilator by surface electrical stimulation of the median nerve using a standard electromyography machine. We hypothesized that any difference in sympathetic innervation to the right and left eye would be accentuated.

Methods:
Ten healthy volunteers tested before and after monocular instillation of brimonidine 0.2% to induce pharmacological Horner syndrome were compared to ten patients with proven Horner syndrome. Pupillary responses were measured with binocular pupillometry (DP-2000, Neuroptics; Irvine, CA) in response to sympathetic activation by electrical stimulation (0.2 ms, 50 mA) of the median nerve in darkness and at various times after extinction of a 3log lux light stimulus (1 vs. 4 seconds). Sudomotor sympathetic responses from the palm were recorded simultaneously.

Results:
In subjects with Horner syndrome or pharmacologically induced unilateral sympathetic deficit, electrical stimulation in combination with the extinction of light greatly enhanced the anisocoria during the evoked pupil dilation and was well tolerated. The asymmetric sympathetic response was greatest when the electrical stimulus was given 1-2 s after termination of the light. Two discernible reflex dilation responses appeared; an initial symmetric dilation due to central inhibition of the Edinger- Westphal nucleus followed by an accentuated asymmetric dilation due to enhanced peripheral sympathetic stimulation.

Conclusions
Electrical sympathetic stimulation given at the termination of a short light stimulus appears to greatly enhance the sensitivity for diagnosing asymmetric pupil dilation due to Horner syndrome. This strategy may improve upon the ability to rule in or rule out a unilateral oculosympathetic deficit, especially if the results of topical pharmacological testing are inconclusive.

M15

Penumbra salvage and infarct growth in acute ischemic stroke: Multiple factors explain high interindividual variability

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Introduction:
Effective treatment of ischemic stroke requires reperfusion of the penumbral brain tissue. We aimed at investigating predictors of penumbra salvage and infarct growth.

Methods:
In the Acute STroke Registry and Analysis of Lausanne (ASTRAL) from 2003 to 2016, we selected all middle cerebral artery (MCA) strokes with availability of a good quality CT-angiography < 24 h and thresholded CT-perfusion. Penumbra salvage (PS) and infarct growth (IG) over 24 hours were correlated in multivariate analyses with clinical, radiological and biochemical variables, and in adjusted analysis with clinical outcome.

Results:
In the 551 MCA strokes included, 49.2% were females, median age ($\pm$ IQR) was 68.7 $\pm$ 21, admission NIHSS 14 $\pm$ 12, and onset-to-imaging time 169.5 $\pm$ 283 minutes. More PS was associated with higher BMI, hemineglect, absence of early ischemic changes, leukoaraiosis and other vascular territory involvement, larger baseline penumbra and a lower clot burden. Less IG was associated with current smoking, lower admission glycemia, larger baseline infarct core, absence of early ischemic changes, chronic vascular brain lesions and other territory involvement, absence of extracranial arterial pathology and hyperdense MCA sign, and lower clot burden. Adding subacute variables to these analyses, recanalisation were associated with more PS and less IG, and the absence of parenchymal haemorrhage with less IG. More PS and less IG were independently correlated with better 12 months functional outcome.

Conclusions:
Penumbra salvage and infarct growth depend on multiple clinical, metabolic, parenchymal, and arterial variables. These findings may explain variability of treatment response and outcome, and may help select patients for late or more aggressive management.

Poster | Posters

P01* - P15*: Kandidaten für den Déjérine-Dubois-Preis

P01* - P15*: Candidats pour le prix Déjérine-Dubois

P01*

Patient satisfaction with the first talk about diagnosis and its impact on treatment decisions: a Swiss Multiple Sclerosis Registry study

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Background and aims:
Patient satisfaction with the first diagnostic consultation (FDC) might have an impact on treatment decision. Initiation of disease modifying treatment (DMT) in multiple sclerosis (MS) should be informed, shared with the patient, and consider all appropriate options.[1] We aimed at investigating factors contributing to patient satisfaction with the FDC and to assess its association with DMT initiation.

Methods:
Using retrospective patient-reported data of the Swiss MS Registry, we fitted ordered logistic regression models (outcomes: a. Satisfaction with FDC: 1 (not at all, reference) to 5 (very satisfied); b. Start of DMT after FDC: no/yes), adjusted for period of diagnosis and other pre-specified confounders. Primary progressive MS was excluded.

Results:
421 persons with MS diagnosed after 1995 (clinically isolated syndrome (11), relapsing remitting (379) or secondary progressive MS (31) at diagnosis) were included. 54% of participants were satisfied with the FDC (levels 4-5), 24% were not satisfied (1-2), and 22% were neutral (3). For 18% the FDC lasted $\leq$ 10 min, for 42% 10-30 min, for 32% $\geq$ 30 min, others did not recall. 84% perceived the diagnosis as clear. The most covered topics were the nature of MS (67%) and DMT (72%). 59% were suggested $\geq$ 2 DMT options, 22% 1 option, and 19% no DMT option. Of all patients, 70% initiated DMT within 3 months, 7% after 3 months, and 23% did not start any. In the multivariable regression on satisfaction with FDC, involvement in the DMT choice (OR 16, 95% CI [4- 59] vs. no involvement), the number of topics covered (1.4 [1.2 -1.7] per additional topic), clarity of the diagnosis (3.5 [1.5-8] vs. a perceived unclear diagnosis), and high socioeconomic status defined by highest work position (2.1 [1.1-4]), were associated with better satisfaction. Worse satisfaction was associated with an interval from contacting a doctor to the diagnosis exceeding 3 months (0.48 [0.27-0.85]). Satisfaction with the FDC (6 [2-19]), diagnosis after 2010 (8.6 [2.1-35.6]), and FDC longer than 30 min (4.9 [1.1-20.7]), were associated with DMT initiation. Males were less likely to start DMT (0.3 [0.1-0.7]).

Conclusions:
Satisfaction with FDC could be crucial for increasing DMT initiation in the MS population. In order to achieve that, physicians should aim to minimize the diagnostic process length, dedicate ample time to the FDC, provide clear information about MS, and involve patients in treatment decision.

P02*

Management of patients with minor clinical deficits despite a large cerebral vessel occlusion

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Background and Purpose:
The optimal management of stroke patients with only minor clinical deficits in spite of an acute large vessel occlusion (LVO) is currently unknown. While pathophysiologic considerations support an early reperfusion therapy of the occluded vessel, those patients were not sufficiently represented in randomized controlled trials and initial medical treatment with rescue-intervention only in case of secondary neurological deterioration is common.

Methods:
In this monocentric retrospective study all patients who underwent mechanical thrombectomy between 01/2013 and 12/2016 at the University Medical Center Erlangen were investigated. Patients with National Institutes of Health Stroke Scale (NIHSS) < 5 on admission were identified and management of these patients was dichotomized according to "acute recanalization" and "initial medical management with rescue-intervention in case of secondary deterioration". Intra-hospital mortality and functional outcome on day 90 using the Modified Rankin Scale dichotomized according to favorable (mRS 0-2) and poor (mRS 3-6) were assessed.

Results:
223 patients (184 (83%) with anterior circulation stroke) were included. Median age was 75 (interquartile range (IQR) 60-80) years, 120 (54%) patients were female. 13 (6%) patients presented with NIHSS < 5 on admission. Rescue-intervention (n=5) was associated with a high rate of poor functional outcome (4 (80%) and a higher intrahospital mortality compared to immediate thrombectomy (n=8) (4 (80%) vs. 1 (13%), p=0.032).

Conclusions:
Initial medical management with rescue-intervention in patients with LVO and minor neurological deficits is associated with a high risk of unfavorable outcome. Timely diagnosis and recanalization of LVO should be considered and prospectively examined even in patients with mild symptoms.

P03*
Systemic review and meta-analysis of haematoma location and morphology of anticoagulation- associated intracerebral haemorrhage

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Introduction:
The location and morphology of intracerebral haemorrhage (ICH) might help to better understand the causes and mechanisms of oral anticoagulant-related ICH (OAC-ICH).

Methods:
We performed a systematic literature research and meta-analysis of studies comparing neuroimaging findings in patients with OAC-ICH compared to those with ICH not associated with OAC (non-OAC ICH). We calculated pooled risk ratios (RRs) for ICH location using the Mantel-Haenszel random-effects method and corresponding 95% confidence intervals (95%CI).

Results:
We identified 8 studies including 6259 patients (OAC-ICH n=1107, pooled OAC-ICH population 21.5%, inter-study-range 1.5% to 39.6%). There was some evidence for deep ICH location (defined as ICH in the thalamus, basal ganglia, internal capsule or brainstem) being less frequent in patients with OAC- ICH (OAC-ICH: 450/1102 vs . non-OAC ICH: 2656/4819; RR 0.94, 95%CI 0.88 -1.00; p=0.05; I2=0%) while cerebellar ICH location was significantly more common in OAC-ICH (OAC-ICH: 111 /1069 vs. non-OAC ICH: 326/4787; RR 1.45, 95%CI 1.12 -1.89; p=0.005; I2=21%) compared to non-OAC ICH. There was no statistically significant relationship to OAC use for lobar (OAC-ICH: 423/1107 vs. non-OAC ICH: 1884/5152; RR 1.02, 95%CI 0.89 -1.17; p=0.75; I2=53%, p for heterogeneity= 0.04) and brainstem ICH (OAC-ICH: 36/546 vs. non-OAC ICH: 172/2626, RR 1.04, 95%CI 0.58 - 1.87, p=0.89, I2=59%, p for heterogeneity = 0.04). The risk for intraventricular extension (OAC-ICH: 436/840 vs. non-OAC ICH: 1429/3508; RR 1.26, 95%CI 1.16 -1.36; p < 0.001; I2=0%) was significantly increased in patients with OAC-ICH.

Conclusion:
The overrepresentation of cerebellar ICH location and intraventricular extension in OAC-ICH might have mechanistic relevance for the underlying arteriopathy, pathophysiology or bleeding pattern of OAC-ICH, and should be investigated further.

P04*
Neuroinflammation may have a beneficial effect on experimental stroke

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Background:
Experimental studies indicate similar molecular mechanisms in cerebral hypoxia and autoimmune neuroinflammation, e.g. invasion of immune cells. This lead to investigations of potential effects of immunomodulatory MS therapeutics on secondary stroke-associated inflammatory damage in experimental and clinical studies. However, mutual interactions of autoimmune, antigen-specific inflammatory reactions and cerebral ischemia have not yet been investigated.

Methods:
Active MOG35-55 experimental autoimmune encephalomyelitis (EAE) was induced in male C57Bl/6 mice. Sham-immunized mice (CFA) served as control group. During different phases of EAE vs. control, transient middle cerebral artery occlusion (tMCAO, 60 minutes) was performed. After 24 h brain tissue was collected and analysed for infarct and edema size and immune cell infiltration.

Results:
In the acute phase, infarct sizes in actively immunized mice inversely correlated with EAE score ($p < 0.005$, $r = -0.52$, $n = 43$). This held similarly true for edema size ($p = 0.006$, $r = -0.32$) and combined damaged tissue (infarct + edema size; $p < 0.004$, $r = -0.5196$). In group comparisons of severely diseased mice (score 5 - 7, $n = 9$) versus both non-diseased but MOG-immunized ($n = 22$) and control mice ($n = 35$) significantly smaller infarct sizes ($p = 0.0018$ and 0.0026) and smaller areas of combined tissue damage ($p = 0.0011$ and 0.0029) could be detected. Histopathological analysis indicated a shift in immune cell infiltration of CD45+ cells 24 h after tMCAO in the ipsilateral hemisphere. No differences were seen for CD3+ T cells or activated microglia. These findings could not yet be corroborated in the chronic phase of EAE (CFA ($n = 11$) vs. MOG ($n = 10$): n.s.). Differences in gene expression are now being analyzed via a multiplex gene expression analysis for 190 genes associated with neuroinflammation and hypoxic damage.

Conclusions:
Our data indicate a very early involvement of immune mechanisms in this experimental model of stroke as antigen-specific CNS autoimmunity appears to have a positive influence on primary tissue damage and edema. This effect seems to be linked to an active CNS involvement of an antigen-specific inflammatory reaction as it could not be detected in both control (CFA) and MOG-immunized mice without disease activity or in the chronic phase of the EAE. This ongoing work will contribute to a better understanding of interactions between CNS autoimmunity and cerebral ischemia.

P05*
Inhibition of c-Jun N-terminal kinase as new therapeutic approach for treatment of multiple sclerosis

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Aim and introduction:
c-Jun N-terminal kinase (JNK) is involved in several immune mechanisms (i) and JNK activation might play a role in pathomechanisms of multiple sclerosis (MS) since it has been shown to be upregulated during relapses in MS patients (ii) and in its animal model, experimental autoimmune encephalomyelitis (EAE), during peak of disease (iii). To investigate the efficacy of JNK inhibition in vitro and in vivo was the aim of our study.

Methods:
Chronic EAE was induced by active immunization with MOG35-55 in female wild type C57BL/6 mice. SP600125 (SP), a reversible ATP-competitive inhibitor of all JNK isoformsi, was given orally (30mg/kg ($n = 9$), 15mg/kg ($n = 10$) or vehicle ($n = 9$)) after individual disease onset (EAE-Score ≥ 2). In vitro we studied the effects of SP 10μM/200μM on Jurkat cells (highly proliferating T cell leukaemia cell line; 3 experiments in triplicates) or SP 10nM/10μM on primary human T cells of healthy donors (stimulation: PHA 2.5μg/ml). Apoptosis after 48 h (3 experiments in triplicates), and proliferation after 72 h (6 experiments in triplicates) were analysed by flow cytometry (AnnexinV/PI-staining; CFSE-staining).

Results:
In vivo, SP ameliorates EAE severity dose dependently (reduction compared to control: 15mg/kg: 25%, $p = 0.05$; 30mg/kg: 44%, $p < 0.0001$; Kruskal Wallis Test). In vitro, SP increased Jurkat apoptosis by 2.2- 2.4-fold (mean ($\pm$ SE): control: 9.0 ($\pm$ 0.32), 10μM: 16.8 ($\pm$ 2.2) ($p = 0.07$), 200μM: 21.9 ($\pm$ 1.3) ($p = 0.001$); Friedman-ANOVA) but not apoptosis of T cells from healthy donors. In contrast, proliferation of human T cells was significantly inhibited by SP (mean percentage ($\pm$ SE): control: 18.5% ($\pm$ 1.2); 10nM: 16.8% ($\pm$ 1.4) ($p > 0.999$); 10μM: 1.9% ($\pm$ 0.6) ($p < 0.0001$), Friedman-ANOVA).

Conclusion:
Our data warrants further investigations on the beneficial mechanism of JNK inhibition in an MS- model. Differences of in vitro findings between primary human T cells and a leukemia T-cell line indicate different susceptibility to JNK inhibition according to activation status. However, further investigations are needed.

P06*
State space velocity: a novel quantitative predictive marker in hypoxic-ischemic encephalopathy

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Introduction:
Due to severe encephalopathy just few patients regain consciousness after cardiac arrest. Outcome prediction is essential in determining further therapeutic interventions. Subjective methods, like the electroencephalogram (EEG) based on visual scoring, is one of the key components in determining prognosis in postanoxic patients. We introduced a model-based approach of EEG analysis (state space model), that allows for a quantitative and non-biased description of temporal EEG variability.

Methods:
Standard EEG recordings from 83 comatose patients after cardiac arrest were retrospectively analyzed. Neurological outcome was assessed one month after cardiac arrest. Aiming to quantify the background variability of EEG

recordings independent from visual EEG scoring we implemented a model-based approach (state space analysis). We then compared state space velocity (i.e. a measure for spectral variability) between groups and correlated mean velocity with clinical outcome parameters and EEG patterns.

Results:
Spectral variability (state space velocity) was significantly different between patients with poor and good outcome after cardiac arrest: Lower mean velocity of temporal electrodes (T4 and T5) was significantly associated with poor prognostic outcome ($p < 0.005$) and correlated with visual EEG markers such as generalized periodic discharges ($p < 0.02$) or burst suppression pattern ($p < 0.03$). Receiver operating characteristic (ROC) analysis confirmed the predictive value of lower state space velocity for poor clinical outcome after cardiac arrest (AUC 80.8, 70% sensitivity, 15% false positive rate).

Conclusion:
Here we introduce a novel quantitative EEG model-based approach for outcome prognostication in postanoxic encephalopathy.

P07*
STRAW-II "STRoke AWareness" - Awareness of Stroke in a small region of Switzerland

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Background and Aim:
Effective therapeutic opportunities with good functional outcome and quality of life are available for ischemic strokes. As "time" is still one of the most relevant factors for successful treatment patient information about stroke symptoms and the correct behaviour in an emergency situation is essential. The aim of STRAW-II was to assess the knowledge about stroke symptoms and therapy in a region in Eastern Switzerland after a 2 year period of public relations aiming to improve the results of STRAW-I. Public relations included a nation-wide media campaign via TV, cinemas and print media supported by the Swiss Heart Foundation as well as regional public events and newspaper advertisements.

Methods:
The survey was conducted from April to June 2017 in 12 different local GP offices. The questionnaire consisted of exactly the same 9 questions as in 2015.

Results:
405 people (169 men, 236 women) aged between 18 and 71 years took part in the survey. The distribution of age and education was comparable with the results in 2015 though less questionnaires were completed in 2017 (405 vs. 550). Again the majority knew the common stroke symptoms like hemiparesis and aphasia and also most of the participants would call 144 (81% vs. 86% in 2015). Compared to 2015 only 17% instead of 24% would see their GP first but unexpectedly 32% would stay with the patient doing nothing (2015 only 1,45%). In case of eye symptoms still 52% (56% in 2015) would contact the ophthalmologist first. Only 46% (60% in 2015) knew about the possibility of acute medical treatment.

Discussion:
Our results show a good knowledge in terms of common stroke symptoms except for eye symptoms. The intention to call 144 is high, but knowledge of acute stroke treatment is low.

Conclusion:
Despite 2 years of effort to improve the populations knowledge about stroke symptoms, the need of a fast transport via 144 to a specialized stroke centre for acute stroke treatment, the results are disappointing.

P08*
Preliminary Experience with a Novel Drug Coating Balloon Catheter for Symptomatic Intracranial High-grade Stenosis

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Aim:
Intracranial arteriosclerotic disease is a relevant cause of ischemic stroke worldwide. Despite best medical treatment, the re-occurrence rate is high. Because of the discouraging SAMMPRIS trial [1], neurovascular treatment remained as a second line therapy. Since, there has been tremendous advance in device technology. SeQuent Please NEO (B.Braun, Melsungen, Germany) is a novel polymer-free, drug coated (paclitaxel/iopromide) balloon (DCB) primarily designed for cardiology. Because of its high flexibility and pushability it seems to be suitable also for intracranial use. Furthermore, it offers a sustained anti-proliferative effect and natural vessel restoration. Additionally, a recent small study of a similar DCB showed promising results [2]. The aim of this case series was to assess feasibility and safety of Sequent Please NEO in symptomatic intracranial high-grade stenosis.

Methods:
A single-center case series of 12 patients with symptomatic intracranial high-grade stenosis between 09/2016–01/2018 treated with SeQeunt Please NEO DCB executed at a tertiary stroke center in Switzerland.

Results:
12 patients (100% men, median ages 73 years (interquartile range (IQR) 70-77) were treated with SeQuent Please NEO. Median pre-treatment carotid stenosis grade was 78% (IQR 75-80) with 2 mid- basilar, 5 internal cerebral artery and 5 vertebral artery lesions. Median post-treatment stenosis grade was 50% (IQR 45-52). Successful angioplasty was achieved in all cases without technical failure and no peri-procedural re-occlusion rates and no mortality rate at follow-up.

Conclusion:
SeQuent Please NEO CDB demonstrates to be feasible and safe in symptomatic intracranial high-grade stenosis. Therefore, it might constitute a promissing alternative to medical treatment.

P09*
Comparison of New-Generation Double-Layer Micromesh Carotid Stent-System versus Carotid Self- expanding Hybrid Stent System in Symptomatic Carotid Artery Stenosis

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Aim:
Carotid artery stenosis is a relevant cause of ischemic stroke. Carotid artery stenting is an emerging alternative treatment option to surgical carotid endarterectomy. Several carotid stent-systems with different stent designs are available. CASPER (MicroVention, Inc., USA) – a double-layer micromesh carotid stent-system designed to prevent peri-procedural embolic release – belongs to the latest generation of carotid stent system. The aim of this study was to assess efficacy and safety of CASPER compared to a carotid self-expending hybrid stent system (Invatec Cristallo Ideal, Medtronic, USA) (Cristallo) in symptomatic carotid artery stenosis (sCS).

Methods:
A single-center, open-label, retrospective cohort study of 57 consecutive patients with proven sCS between 01/2014–08/2017 executed at a tertiary stroke center in Switzerland. Outcome measures were i) good clinical outcome at 90 days (mRS < 2), ii) peri-procedural complications and ischemic events iii) re-occlusion rate and iiii) mortality within 30 days.

Results:
22 patients (23% women, median age 75 years (interquartile range (IQR) 71-80) were treated with CASPER, 35 patients (29% women, median age 71 years (IQR 63-76) years) with Cristallo. In both groups, pre-treatment carotid stenosis had similar median NASCET score of 80%. Successful deployment was achieved in all cases without technical failure and similar re-occlusion rates and mortality rate within 30 days. Clinical outcome was similarly beneficial in both groups. In the Cristallo group peri-procedural ischemic event was insignificantly higher (3 vs 0; p=0.16).

Conclusion:
CASPER and Cristallo demonstrate to be similarly effective and safe in symptomatic carotid artery stenosis.

P10*
Reasons for Prehospital Delay in Acute Ischemic Stroke: a Prospective Cohort Study

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Introduction:
Prehospital delays jeopardize the chances for patients with acute ischemic stroke (AIS) to be treated with recanalization therapies. Population-based education campaigns aiming at reducing prehospital delay are expensive and of questionable benefit. The aim of this study was to understand the reasons leading to prehospital delays in AIS.

Methods:
In this prospective cohort study, we included patients with AIS admitted to the Stroke Center of the University Hospital Basel between 2015 and 2017. AIS had to be confirmed on Diffusion-Weighted MRI. Trained study nurses and physicians interviewed patients and their proxies at bedside along a standardized 28-item questionnaire on the prehospital phase. Prehospital delay was defined as delay >4.5 hours between AIS onset and admission to the University Hospital Basel.

Results:
Overall, 337 patients were enrolled, of which 140 (42%) reached the University Hospital Basel with a prehospital delay, while 197 (58%) arrived on time. In multivariate analysis, risk factors for prehospital delay were a prehospital visit to the family doctor (OR 3.49, 95%-CI 1.54-7.93, P < 0.01); lack of knowledge about stroke symptoms (OR 3.98, 95%-CI 2.32-6.72, P < 0.01); living alone (OR 1.84, 95%- CI 1.09-3.11, P = 0.02), and low NIHSS (OR 0.91, 95%-CI 0.86-0.98, P = 0.01). Lack of knowledge about stroke was associated with diabetes mellitus (OR 2.28, 95%-CI 1.21-4.27, P = 0.01), but not with a history of prior stroke (OR 0.62, 95%-CI 0.36 -1.08, P = 0.09).

Conclusion:
In this contemporary cohort, prehospital delay was frequent. Two of the recognized main risk factors of

prehospital delay are modifiable, i.e. prehospital visit to the family doctor and lack of knowledge on stroke. Family doctors should be seen as partners to reduce prehospital delays, and information campaigns targeting family doctors may contribute reducing prehospital delay. Of note, knowledge on stroke was not higher among patients with history of a prior stroke. This finding underscores the need for improved information to hospitalized patients with AIS regarding the importance of avoiding prehospital delay in case of a recurrent stroke.

P11*
Papilledema or Papillitis? - Case report: A rare presentation of Neurosyphilis

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A 36-year-old lean man presented with recurrent, transient episodes of visual field defects in the right eye for 6 days. The episodes started suddenly and showed an increase in frequency. The defects involved small spots in different locations or the whole upper visual field of the eye lasting only 30 to

60 seconds. He complained of no other symptoms, especially no headache. He had an unexplained rash on the whole body 4 weeks ago which resolved without intervention. His medical history revealed only sport injuries and a slight weight loss due to lifestyle modifications.

The neurological examination was normal, but fundoscopy showed bilateral optic disc swelling marked on the right. Ophthalmologic exploration revealed enlargements of the blind spots, but otherwise normal findings with a visual acuity of 1.0, normal colour vision and normal pupillary reflexes, corresponding to the diagnosis of papilledema. Intracranial hypertension was assumed. Brain imaging (CCT and in the follow up MRI) was normal. Lumbar puncture revealed normal CSF pressure, but a slight pleocytosis (9 cells/mcl) with normal protein.

Further anamnesis revealed homosexuality with promiscuity in the past 6 months and a travel to South America.

Additional serology testing showed highly positive results for an active neurosyphilis stadium II (TPPA 1:10240, Treponema RPR 1:16). The previous exanthema and ocular syphilis confirmed stadium II. He was treated with Penicillin and his visual disturbances improved rapidly.

Conclusion:
This case shows a rare presentation of neurosyphilis with clinical signs of papilledema. In the context of the syphilis, it was a papillitis and not papilledema. Apart from that, it underscores the necessity of a detailed anamnesis, including social and sexual aspects. While at the beginning of the 20 th century syphilis was the main cause of inflammatory eye infections, syphilis has become rare. However, since 2002 cases increased in Switzerland. Therefore DD of syphilis should be taken into account in patients with papilledema/optic neuritis.

P12*
The impact of collaterals on reperfusion in stroke

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Aim:
Despite improvements in acute recanalization treatments, stroke remains one of the leading causes of death and disability worldwide. In order to achieve the best outcome possible for the individual patient, therapies have to be administered rapidly. Here, we propose that 1) treatment success relies on collateral flow to the ischemic area, and that 2) dynamic changes in cerebral blood flow (CBF) go beyond the ischemic area, affecting the contralateral side of stroke as well. Furthermore, we hypothesize that CBF changes within and outside the affected territory may predict stroke outcome.

Methods:
For induction of experimental ischemia in two mouse strains with differences in the naive collateral network, thrombin was injected into the middle cerebral artery (MCA) of C57BL/6 and Balb-C mice. 30 min later, thrombolysis was initiated through intravenous injection of recombinant tissue plasminogen activator (rt-PA). CBF was monitored using laser speckle imaging during stroke and repeatedly until d7. Functional deficits were assessed by the sticky tape test and a composite neurological score. After final imaging and functional assessment on day 7, cardiac ink perfusion was used for visualization of blood vessels and Triphhenyl tetrazolium chloride (TTC) for infarct size quantification.

Results:
In mice with poor collaterals (Balb-C), stroke led to a persisting CBF drop. Spontaneous reperfusion was detected in few mice with good collaterals (C57BL/6). In both strains, rt-PA administration at 30 minutes after stroke improved reperfusion. Interestingly, blood flow was highly dynamic during ischemia and reperfusion, involving not only the ipsilateral hemisphere and leptomeningeal collaterals, but also contralateral areas. The administration of rt-PA reduced infarct volume and sensorimotor deficits. We are currently analyzing the whole spectrum of CBF recordings throughout day 7 to further delineate changes in perfusion and their impact on outcome in the different strains.

Conclusion:
This is the first study demonstrating remote changes in cerebral blood flow in an experimental ischemia model including clot formation and thrombolysis, closely mimicking the situation in stroke patients. Based on our preliminary data, CBF dynamics are different in mice with a good versus poor collateral network. Remote CBF signal may be a novel predictor of stroke outcome. Further analyses are under way.

P13*
Crossed Cerebellar Diaschisis after stroke: a vascular phenomen?

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Background and Aims:
Crossed cerebellar diaschisis (CCD) in internal carotid artery (ICA) territory stroke refers to a reduction in blood flow and energy metabolism in the contralateral cerebellar hemisphere. CCD may be due to interruption of cerebrocerebellar tracts, a clear clinical correlate of CCD is lacking. Previously we have seen that in patients with ICA occlusion, compensatoriy hemodynamic factors may also influence perfusion in remote brain areas, including the posterior circulation. Parients with large vessel occlusion tend to have a higher risk of a recurrent ischemia if hemodynamic compensation is insufficient and cerebrovascular reactivity (CVR) is reduced. Our goal was to identify potential hemodynamic contributions of CCD in patients with ICA occlusion, using BOLD-CVR imaging and Transcranial Duplex sonography (TCD)

Method:
Duplex sonography and clinical data from stroke patients with unilateral ICAO who underwent blood oxygen level dependent (BOLD)-MRI cerebrovascular reserve (CVR) assessment were analysed. The presence of CCD (either CCD+ or CCD-) was inferred from BOLD-CVR.

Results:
Eightteen patients (10 CCD +/8 CCD -) were included. Stroke deficits on admission were more severe in the CCD+ group. Flow velocities in the P2 segment of the posterior cerebral artery (PCA) in CCD+ vs. CCD- patients were 76 vs. 50 cm/s ipsi- and 76 vs. 49 cm/s contralaterally ($p = 0.03$ and 0.04). Also flow velocities in the P1 segment contralaterally were significantly higher 85 vs. 49 cm/s ($p = 0.002$). All other duplex parameters were similar between both groups.

Conclusion:
In patients with stroke due to ICA occlusion, the presence of CCD indicated 1) more severe stroke deficits on admission and 2) higher flow in both P2 segments and contralateral P1 segment of the PCA. The latter is likely to indicate increased compensatory collateral recruitment through leptomeningeal and PCA collaterals. Our data suggest that in patients with ICA occlusion, there may be an additional hemodynamic contribution to CCD, indicating a more severe hemodynamic compromise.

P14*
Eligibility for late thrombectomy using DAWN, DEFUSE-3 and more liberal selection criteria in a comprehensive stroke center

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Introduction:
Efficacy of late endovascular thrombectomy (EVT) has recently been demonstrated for selected, anterior proximal occlusive stroke in DAWN and DEFUSE-3 trails. However, the proportion of acute ischemic stroke (AIS) patients eligible to such treatment in real life is poorly known. We aimed to identify the eligibility for late EVT at an endovascular-capable stroke center using DAWN, DEFUSE-3, and more liberal clinical-imaging mismatch criteria.

Methods:
All consecutive AIS patients from the Acute STroke Registry and Analysis of Lausanne (ASTRAL) between 2003 to 2017 were selected if they had all necessary DAWN and DEFUSE-3 eligibility dataset. In this cohort we searched for late EVT eligibility according to trials (DAWN and/or DEFUSE-3) criteria. Moreover, we applied more liberal criteria, including pre-stroke Rankin=2, proximal M2 and basilar occlusions, ASPECTS-based core estimation and lower NIHSS cut-offs.

Results:
Out of 1'705 AIS patients arriving between 5-23 h (23% outside referrals) during the study period, 907 had sufficient data for the eligibility analysis. Proportion of late EVT eligible patients varied from 2.2% according to DAWN criteria to 5.3% according to DEFUSE-3 criteria. Applying more liberal criteria, a total proportion of 11.1% was eligible for late EVT in our comprehensive stroke center. Since 2003, late-EVT was effectively performed in 60 patients (mostly following liberal criteria). The proportion of effective late EVT increased from 6% during the 5 years before to 21% since the DAWN results (+250%).

Conclusions:
The eligibility for late EVT varies greatly according to the referral pattern and selection criteria. Of late arriving stroke patients over 15 years at our stroke center, only 5% are eligible for thrombectomy according to DAWN and/or DEFUSE-3 criteria. With more liberal clinical-imaging mismatch criteria, the eligibility proportion reaches 11%. The observed increase of 250% effectively treated patients at our center after the DAWN results suggests an important potential of treatable patients.

P15*
Sensorimotor stroke alters hippocampo-thalamic network activity: A Manganese-enhanced Magnetic Resonance Imaging study

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Aims:
Many stroke survivors suffer from transient or permanent post-stroke cognitive impairment, often representing an insurmountable obstacle on the path to independence in daily life. The mechanisms behind these symptoms remain unclear, as size or location of the ischemic lesion do not reliably predict timing or extent of the cognitive deficit. Particularly the substrate of episodic memory impairment after stroke remains obscure, since hippocampal and parahippocampal areas are usually spared from the infarcted area. Alteration of memory processing networks remote from the ischemic brain region might be responsible for the observed clinical symptoms. In our study, we aimed to characterize changes in hippocampal pathways after sensorimotor stroke by mapping its functional connections using manganese-enhanced MRI (MEMRI) in a rat middle cerebral artery occlusion (MCAO) model along with behavioral and histopathological analysis.

Methods:
Rats were subjected to 60 min MCAO or SHAM surgery. Sensorimotor and cognitive deficits were assessed during a 4-week period using the sticky tape test, an 18-point composite neurological score and the novel object recognition test (NORT). After 28 days and a first MRI evaluation, MnCl2 was injected into the entorhinal cortex and MRI repeated after injection and 1 day later. Rats were then sacrificed and immunohistochemical staining with NeuN, GFAP and DCX was performed.

Results:
Stroke induced sensorimotor and cognitive deficits up to 28 days after MCAO. MRI showed that direct hippocampal injury occurred in some rats, but was no prerequisite for cognitive impairment. MEMRI showed normal Mn2+ distribution in SHAM rats along the hippocampal formation and the fimbriae of the hippocampus to the lateral septal nuclei. In MCAO rats, MEMRI revealed a disturbed Mn2+ signal pattern, including accumulation of Mn2+ in the ipsilateral thalamus. Histopathological analysis showed significant gliosis in this area.

Conclusion:
Our study provides in vivo evidence that remote sensorimotor stroke modifies the activity of hippocampal-thalamic networks. In addition to potentially reversible alterations in signaling of these connections, we suggest that secondary degeneration of the thalamus due to reduced thalamo-cortical input after stroke could reinforce dysfunction of hippocampal-thalamic circuitries. Further studies should investigate whether activation of thalamo-cortical inputs by rehabilitation could improve cognitive deficits after stroke.

P16
A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Effect of Erenumab on Exercise Time During a Treadmill Test in Patients with Stable Angina

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Objectives:
To evaluate the effect of erenumab on exercise capacity in patients with stable angina.

Background:
The relative importance of the CGRP receptor pathway among other mediators of vasodilation in the setting of myocardial ischemia has not been established.

Methods:
Randomized (1:1, erenumab 140 mg or placebo IV), double-blind, controlled study in patients with stable angina due to documented coronary artery disease. Randomization stratified by baseline total exercise time (TET) defined as average TET of two screening exercise treadmill tests (ETT). A final ETT was conducted on Day 1 after administration of study drug. Primary endpoint was change from baseline in TET with a non-inferiority margin of –90 seconds, analyzed using analysis of variance with treatment, randomization strata, age, and sex as covariates. Secondary endpoints included time to onset of $\geq$1 mm ST-segment depression and time to onset of exercise-induced angina. Safety follow-up occurred over 12 weeks.

Results:
Eighty-nine patients enrolled. LS mean (SE) change in TET was –2.9 [14.8] seconds in the erenumab group and 8.1 [14.4] seconds in placebo; adjusted mean (90% CI) treatment difference was –11.0 (– 44.9, 22.9) seconds. The CI lower bound (–44.9 sec) did not reach pre-defined non-inferiority margin of –90 seconds, demonstrating that TET change in the erenumab group was non-inferior to placebo and supporting the hypothesis that erenumab does not decrease exercise capacity versus placebo. No difference observed between erenumab and placebo for time to onset of either exercise-induced angina (hazard ratio [90% CI: 1.11 [0.73, 1.69], p=0.69) or ≥1 mm ST-segment depression (hazard ratio [95% CI]: 1.14 [0.76, 1.69], p=0.59). Adverse events reported by 27% of erenumab-treated patients and by 32% of placebo patients.

Conclusions:
Erenumab did not adversely affect exercise time in at-risk patients with stable angina, supporting that inhibition of the CGRP receptor does not aggravate myocardial ischemia.

P17
Use of Acute Headache and Migraine Medications in Patients with Episodic Migraine in the STRIVE Phase 3 Trial of Erenumab for Migraine Prevention

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Objective:
To analyze (A) change in acute headache medication days/month (AHM, including acute migraine- specific medications (AMSM) as well as paracetamol, NSAIDS etc.) in the overall population as 97.7% used AHM during baseline; (B) change in AMSM days/month in the subgroup who used AMSM during baseline.

Background:
Erenumab is a fully human monoclonal antibody that selectively inhibits the calcitonin gene-related peptide (CGRP) receptor. In the STRIVE placebo-controlled Phase 3 trial (NCT02456740), erenumab 70 mg and 140 mg administered subcutaneously to patients with episodic migraine (EM) significantly reduced monthly migraine days versus placebo. Erenumab also reduced the number of days/month on which patients used AMSM, versus placebo.

Design/ Methods:
Patients recorded medication use with a daily eDiary throughout the 4-week baseline period and subsequent 6-month double-blind treatment period. The number of days/month on which AMSM and AHM were taken was calculated. Change from baseline was analyzed using a linear mixed effects model including covariates of treatment, visit, treatment by visit interaction, stratification factors (region and migraine prophylaxis medication status), and baseline value. Nominal p-values were provided without multiplicity adjustment.

Results:
During baseline, the mean number of AHM days/month in the overall population was 6.91, 6.58, and 6.60 in the placebo, erenumab 70 mg, and 140 mg groups, respectively. Erenumab significantly reduced AHM days/month versus placebo from Month 1 onward. (B) Mean number of AMSM days/month in patients who used AMSM during baseline was 5.68, 5.67, and 5.67 in the placebo, erenumab 70 mg, and 140 mg groups, respectively. Erenumab significantly reduced AMSM days/month versus placebo; mean (95% confidence interval) treatment difference −1.57 days (−2.04, −1.10; $p < 0.001$) for 70 mg and −2.30 days (−2.77, −1.83; $p < 0.001$) for 140 mg, averaged over Months 4−6.
Conclusion:
Erenumab significantly reduced both AHM and AMSM days/month versus placebo in patients with EM.

P18
Erenumab Safety Among Migraine Patients Using Triptans or With Cardiovascular (CV) Risk Factors

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Objective:
To assess erenumab safety by triptan/ergotamine use or cardiovascular (CV) risk.

Background:
Erenumab is the only fully human monoclonal antibody in development specifically targeting the CGRP receptor to prevent migraine. As CGRP can mediate vasodilation, inhibiting the CGRP pathway may carry a theoretical CV risk. Here we assess the safety of erenumab in patients with CV

risk factors or in patients using triptans/ergotamines (which are known to have vasoconstrictive effects).

Design/Methods:
12-week integrated safety analysis of patients in phase 2/3 clinical trials (NCT02066415, NCT01952574, NCT02456740, NCT02483585) who received $\geq$ 1 dose of placebo or erenumab (7-, 21-, 70-, 140 mg). We report treatment-emergent adverse events (AE) in 2 groups: triptan/ergotamine users and patients with preexisting CV risk factors (0, 1, $\geq$ 2).

Results:
Overall, 66.2% (n=690/1043) of placebo and 65.5% (n=1056/1613) of erenumab-treated patients used migraine medications (primarily triptans [> 99%]). AE incidence was similar between treatment groups and triptan/ergotamine users (49.6% placebo, 47.4% erenumab) and non-users (47.9% placebo, 47.2% erenumab). Serious AE incidence for triptan/ergotamine users was 1.9% placebo, 1.7% erenumab, and for non-users, 0.8% placebo, 0.5% erenumab. At baseline, 29.7% and 28.2% of placebo and erenumab- treated patients had 0 CV risk factors, respectively, 40.6% and 41.7% had 1 CV risk factor, and 29.7% and 30.1% had $\geq$ 2 CV risk factors. AE incidence was similar between groups for 0 CV risk factors, (47.4% placebo, 44.8% erenumab), 1 CV risk factor (46.3% placebo, 46.4% erenumab), or $\geq$ 2 CV risk factors (54.2% placebo, 51.1% erenumab). Cardiac (< 2.0%) or vascular AE incidence ($\leq$ 2.3%) was similar among CV risk subgroups and treatment groups, as was SAE incidence (< 2.0%). No dose relationship was observed with triptans/ergotamines or CV risk.

Conclusions:
AEs, including CV AEs, were similar between erenumab and placebo in triptan/ergotamine users and in those with CV risk factors.

P19
Tolerability and Quality of Life in Patients with Multiple Sclerosis Switched to Intramuscular Interferon Beta 1a Autoinjector (Avonex® Pen™): SFERA Study

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Background:
New strategies to minimize and manage drug-related side effects are of major interest to improve quality of life (QoL), promote adherence to therapy, and achieve better outcomes.

Methods:
Prospective, single-arm, open-label, multi-center, non-interventional Phase IV study to evaluate tolerability, treatment satisfaction, QoL and fatigue over 1 year in patients with stable multiple sclerosis (MS) switched from Rebif®, Betaferon®, Extavia®, or Copaxone® to Avonex® Pen™ due to bothersome injection site reactions. Primary endpoint was change in injection site tolerability from baseline to month 4 (100 point-visual analogue scale, 100VAS). Secondary endpoints included change (100VAS) in injection site tolerability, systemic tolerability, treatment satisfaction, QoL (SF-36) and fatigue (FSMC) from baseline to month 12. Exploratory endpoints included the proportion of patients with clinical (no relapses, no disability progression) and radiological ($\leq$2 new T2, no enhancing brain lesions) stability at 12 months. Patients received quarterly neurological examination and yearly brain MRI, and completed study questionnaires and scales over 1 year-follow up. Clinical as well as demographic data were retrieved from patients' records.

Results:
40 patients were enrolled [30 females; mean (SD) disease duration 9.30 (7.079) years; previous therapies: 73% interferon beta1, 27% glatiramer acetate]. At months 4, injection site tolerability improved by a mean of 22.53 points (95%CI 14.45, 30.60, p = 0.00003). At month 12, injection site tolerability, systemic tolerability and treatment satisfaction also improved by a mean of 17.74 (95%CI 9.01, 26.47, p = 0.002), 12.58 (95%CI 0.54, 24.61, p = 0.041), and 23.36 (33.22; 95%CI 11.59, 35.14, p = 0.0003) points, respectively. No significant changes were reported in the physical as well as mental components of SF-36 and in the FSMC scores [mean difference: 1.93 (95%CI -0.26, 4.13, p = 0.117); - 0.43 (95%CI -2.71, 1.84, p = 0.596), and -1.73 (95%CI -4.64, 1.18, p = 0.698), respectively]. 9.1% and 33.3% of patients showed clinical and radiological activity, respectively.

Conclusion:
Avonex® Pen™ represents an alternative treatment option for those patients suffering from intolerable injection-related site effects during high frequency- injectable MS therapies. This benefit should be balanced against the risk of an increased clinical and radiological activity.

P20
Acetazolamide-responsive episodic ataxia linked to novel splice site variant in FGF14 gene

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Aim:
We present a patient with episodic vertigo and dizziness accompanied by persistent mild cerebellar symptoms that

was suspected for episodic ataxia (EA) type 2, but eventually received a diagnosis of spinocerebellar ataxia (SCA) 27, which is usually associated with progressive cerebellar loss-of- function.

Case description:
Episodes were triggered by high stress levels, physical activity, certain body positions (e.g. bending forward) and caffeine intake, lasting between few minutes to several hours, usually accompanied by nausea and sometimes resulting in vomiting. The family history was negative for heredoataxias as well as other neurodegenerative disorders. On clinical examination interictally the patient presented with gaze-evoked nystagmus and rebound nystagmus and slight dysarthria. MRI of the brain was normal and peripheral-vestibular function was bilaterally intact. Based on genetic testing (episodic ataxia panel), a heterozygote splice site variant in intron 1 of the FGF14 gene was identified. A treatment trial with acetazolamide (500 mg per day) was started, resulting in a marked reduction of the frequency (from roughly two to four times per month to once per month) and intensity of the vertigo attacks.

Conclusion:
This report adds important new evidence to previous observations that pathogenic variants in the FGF14 gene may result in variable phenotypes, either in progressive spinocerebellar ataxia (type 27) or in episodic ataxia as in our case. Our patient responded well to acetazolamide (reduction in the frequency of attacks by about two thirds), supporting the hypothesis of a sodium channelopathy.

P21
Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Primary Progressive Multiple Sclerosis

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Background:
Ongoing safety reporting on disease-modifying therapies for multiple sclerosis (MS) is crucial to understanding the long-term benefit–risk profile. Data are reported from patients receiving ocrelizumab in one Phase II study in relapsing-remitting MS (RRMS; NCT00676715), two identical Phase III trials in relapsing MS (RMS; OPERA I/II [NCT01247324]/[NCT01412333]) and the Phase III trial in primary progressive MS (PPMS; ORATORIO [NCT01194570]) and their extensions.

Aim:
To report ongoing safety evaluations from ocrelizumab clinical trials and open-label extensions (OLEs) up to September 2017.

Methods:
Ocrelizumab recipients received 600 mg doses intravenously every 24 weeks in OPERA I/II (96 weeks; first dose: 2×300 mg infusions split by 14 days) and ORATORIO ($\geq$ 120 weeks; all doses split). Patients in the Phase II study received 600 mg or 2000 mg infusions through Week 24 (both doses split); treatment through Week 96 was ocrelizumab 600 mg (patients starting on 600 mg dose and those receiving placebo or interferon beta-1a, 30 μg) or 1000 mg (those starting on ocrelizumab 2000 mg). Comparators were placebo (ORATORIO and Phase II) and interferon beta-1a (44 μg subcutaneous/three times weekly [OPERA] or 30 μg intramuscular/weekly [Phase II]). Patients completing controlled-treatment periods could enroll in the OLE with ocrelizumab 600 mg / 24 weeks. Data presented are from ocrelizumab recipients including those switching from comparators. Long- term safety data will continue to be reported on a regular basis.

Results:
As of February 2017, 2,301 patients with MS received ocrelizumab, resulting in 7,748 patient-years of exposure. Reported rates per 100 patient-years (95% confidence interval) were as follows: adverse events (AEs), 226 (222-229); serious AEs, 7.18 (6.59-7.80); infections, 71.3 (69.5-73.2); serious infections, 1.86 (1.57-2.19); and malignancy 0.454 (0.316-0.632). Updated cross-trial information using a September 2017 data-cut will be presented.

Conclusions:
The updated safety profile in the ocrelizumab MS all-exposure population is generally consistent with that seen during the controlled-treatment period in the RMS and PPMS populations.

P22
Annualized Relapse Rate and Confirmed Disability Progression in Patients Receiving Continuous Ocrelizumab or Switching From Interferon beta-1a to Ocrelizumab in the OpenLabel Extension Period of the Phase III Trials of Ocrelizumab in Patients With RMS

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Background:
The efficacy and safety of ocrelizumab (OCR) in relapsing multiple sclerosis (RMS) were demonstrated in the 96-week double-blind control period of OPERA I and II (NCT01247324; NCT01412333).

Aim:
To assess the efficacy of switching to or maintaining OCR therapy on clinical measures of disease activity and progression in the open-label extension (OLE) period of Phase III trials in RMS.

Methods:
At the start of the OLE period, patients continued (OCR-OCR) or were switched from interferon (IFN) β-1a to OCR (IFN-OCR). Adjusted annualized relapse rate (ARR), time to onset of 24-week-confirmed disability progression (CDP24) and change in adjusted mean Expanded Disability Status Scale (EDSS) score from baseline were analyzed.

Results:
More than 89% of patients completed OLE Year 2. Among IFN-OCR patients, ARR decreased from 0.20 in the year pre-switch to 0.10 and 0.08 at Years 1 and 2 post-switch ($p < 0.001$ Year 1 versus pre-switch; $p = 0.31$ Year 1 versus Year 2). OCR-OCR continuers maintained the low ARR through the year pre-OLE and the 2 years of the OLE period (0.13, 0.11 and 0.08). OCR-OCR continuers versus IFN-OCR switchers had lower proportions of patients with CDP24 in the year pre-switch and Years 1 and 2 of the OLE period (7.7%/12.0%, 10.1%/15.6% and 13.8%/18.1%; $p < 0.05$, all difference comparisons). OCR- OCR continuers versus IFN-OCR switchers had a larger decrease in mean EDSS score from baseline, at pre-switch and Years 1 and 2 of the OLE period (–0.15/0.03, –0.12/0.01 and –0.06/0.04; all $p < 0.01$, Year 2 $p = 0.06$).

Conclusions:
Switching from IFN β-1a to ocrelizumab at the start of the OLE period was associated with a rapid and robust reduction in ARR which was maintained through the 2-year follow-up of the OLE period. The benefits of ocrelizumab on ARR and CDP24 as seen in the 2-year double-blind controlled period were maintained after 2 years in the OLE period.

P23
Une brève histoire des blocs de conduction nerveux

F Ochsner

Cabinet médical Dr méd. François Ochsner

Introduction:
La description électrique des blocs de conduction nerveux (BC°) et leur importance physiopathologique a émergé récemment dans l'évolution des concepts électro-cliniques.

Méthodes:
L'histoire du concept de BC° est retracée en utilisant les données bibliographiques et les témoignages des acteurs plus récemment impliqués dans leur découverte.

Résultats - Discussion:
L'histoire de la mesure des vitesses de conductions nerveuses débute vers 1850 par les travaux de Hermann von Helmholtz (1821-1894). À la fin du XIXe siècle, Silas Weir Mitchell (1829-1914) et Wilhelm Erb (1840-1921) repèrent le rôle d'une lésion fonctionnelle focale sur un nerf, suffisante pour suspendre la conduction pendant plusieurs semaines mais sans dégénérescence associée. La méthode anatomo-clinique s''intéresse peu à ce concept sans lésion visible. La Deuxième Guerre mondiale et son lot de blessures nerveuses réactive l'intérêt physiopathologique. En 1942, la classification des lésions nerveuses de Herbert J. Seddon (1903-1977) fait apparaître les notions de transcient block et de neurapraxia. L'intérêt tardif porté à l'amplitude des réponses dans l'histoire de l'électrophysiologie ralentit cependant la connaissance des blocs. Le lien entre démyélinisation et BC° émerge progressivement dans les années 1950-60 en particulier grâce aux travaux de W. I. McDonald (1933- 2006). Les progrès technologiques des appareils permettent ensuite de détecter plus précisément les BC° et améliorent les critères diagnostiques des polyradiculoneuropathies. La valeur physiopathologique des BC° émerge finalement dans les années 1970. À Genève, Gérard Roth (1923- 2006) utilise une méthode de stimulation distale et proximale des nerfs avec une électrode monopolaire. Une classification est proposée en

blocs 1) rapidement réversibles, 2) de durée plus prolongée (2-4 mois) et 3) de longue durée (> 4mois) (Ochsner, 1988). Parmi ces derniers, sont distingués les blocs prolongés et persistants. De nouvelles entités sont décrites comme les neuropathies multifocales sensitivo-motrices (Lewis et al. 1982), motrices pures (Roth el al. 1986), HNPP (Roth 1978) et post-actiniques (Roth 1988).

Conclusion:
Le concept de BC° est revenu très fortement d'actualité depuis 2013 avec la description des nodopathies et paranodopathies (Uncini et al. 2013). Un nouveau pas dans la compréhension de la physiopathologie des BC° a été franchi.

P24
Suppression of MRI Dsease Activity and Slowing of Brain Volume Loss Over 7 Years in Alemtuzumab- Treated Patients with Active RRMS: CARE-MS I (TOPAZ Study)

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Aims:
In CARE-MS I (NCT00530348), alemtuzumab (12 mg/day, baseline: 5 days; 12 months later: 3 days) demonstrated significant improvements in MRI outcomes, and reduced brain volume loss (BVL), versus subcutaneous interferon beta-1a (SC IFNB-1a) over 2 years (y) in treatment-naive patients with active relapsing-remitting MS (RRMS). The efficacy of alemtuzumab was maintained in a 4-y extension (NCT00930553; 93% enrolled; 85% completed), with 63% of patients receiving no additional alemtuzumab or disease-modifying therapy (DMT) after the initial 2 courses through Y6. In the extension, patients could receive additional courses of alemtuzumab as needed for disease activity or receive other DMT per investigator's discretion. Following this extension, patients could enrol in the ongoing 5-y TOPAZ study (NCT02255656) for further evaluation. Here we present the effects of alemtuzumab over 7 y (2-y core study plus 4-y extension plus 1 y of TOPAZ) on MRI disease activity and BVL in CARE-MS I patients.

Methods:
At investigator discretion, patients in TOPAZ can receive additional as-needed alemtuzumab (≥ 12 months apart; no criteria), or receive another DMT (at any time). Annual assessments include MRI disease activity (scored as: new gadolinium [Gd]-enhancing lesions; new/enlarging T2 hyperintense lesions), new non-enhancing T1 hypointense lesions, and BVL (derived by relative change in brain parenchymal fraction [BPF]).

Results:
Of the 376 patients who received alemtuzumab in CARE-MS I, 349 (93%) entered the extension; 299/376 (80%) CARE-MS I patients completed Y1 of TOPAZ (Y7 after initiating alemtuzumab). 59% received neither additional courses of alemtuzumab nor another DMT through Y7. At Y7, 68% of patients were free of MRI disease activity, 91% were free of new Gd-enhancing lesions, 68% were free of new/enlarging T2 lesions, and 85% were free of new non-enhancing T1 hypointense lesions. Median cumulative BPF change from baseline was –0.59%, –0.87%, –0.98%, –1.13%, –1.37%, –1.43%, and –1.62% in Y1–7, respectively. Median annual BPF change was significantly reduced versus treatment with SC IFNB-1a over 2 y ($P < 0.0001$), remaining low in Y3–7 (Y3: –0.19%, Y4: –0.14%, Y5: –0.20%, Y6: –0.17%, Y7: –0.16%).

Conclusion:
Alemtuzumab reduced MRI disease activity and slowed BVL through Y7, despite 59% receiving no additional treatment since the initial 2 courses. These outcomes were maintained in treatment-naive patients over 7 y in the absence of continuous treatment.

P25
Benefits of Successful Reperfusion in Patients Presenting with ASPECTS 0-5

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Background:
It is not yet known whether mechanical thrombectomy is beneficial in patients with anterior circulation large-vessel occlusion (LVO) presenting with Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 0–5.

Method:
Data from the multicenter Bernese-European RegistrY for ischemic stroke patients treated Outside current guidelines with Neurothrombectomy Devices using the SOLITAIRE™ FR With the Intention For Thrombectomy (BEYOND-SWIFT, NCT03496064) were analyzed. The effect of successful reperfusion on outcome parameters was evaluated in patients presenting with ASPECTS 0–5 using multivariable logistic regression. Results were displayed as adjusted odds ratios (aOR) with 95% confidence intervals (95% CI). Primary outcome was defined as modified Rankin Scale (mRS) 0–3 ('favorable outcome'). Secondary outcomes consisted of mRS 0–2 ('good outcome'), all-cause mortality, and symptomatic intracranial hemorrhage (sICH).

Results:
Of 2046 patients included in this registry, 237 presented with anterior circulation LVO and ASPECTS 0–5. In this subgroup, successful reperfusion was associated with favorable outcome (aOR 5.534, 95% CI 2.363 – 12.961), good outcome (aOR 5.583, 95% CI 1.964 – 15.873), reduced mortality (aOR 0.180, 95% CI 0.083 – 0.390) and lower rates of sICH (aOR 0.235, 95% CI 0.062 – 0.887). No statistically significant interactions between these associations and age groups were found (P for interaction >0.05). The mortality-reducing effect remained statistically significant when analysis was confined to patients with ASPECTS 0–4 (aOR 0.167, 95% CI 0.056 – 0.499). Compared to patients with anterior circulation LVO and ASPECTS 6 - 10, intervention in patients with ASPECTS 0 - 5 were less often successful (86.8% versus 69.9%, P < .001), but rates of sICH were comparable (7.2% versus 6.0%, P = .466).

Conclusion:
Indirect evidence from a large multicenter registry supports the notion that achieving successful reperfusion in patients presenting with ASPECTS 0–5 is beneficial without putting patients at increased risk of sICH. While the data does not allow for general treatment recommendations, formal testing of the best treatment approach (i.e. mechanical thrombectomy versus best medical treatment) in these patients in a randomized controlled trial appears justified.

P26

Fast and fully-automated, deep learning-based brainstem segmentation method provides accurate and reliable brainstem segmentation in Multiple Sclerosis

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Introduction:
The brainstem (BS) as the anatomic link between brain and spinal cord is responsible of vital functions and can be affected by neurodegenerative diseases. Atrophy is a hallmark of neurodegeneration in Multiple Sclerosis (MS) that can be quantified by MRI. So far there is not much known about BS atrophy in MS.

Aims:
To assess accuracy and reproducibility of a fully-automated deep learning-based segmentation method for BS volumetry in 3D high-resolution T1w MRI data of healthy controls (HC) and MS patients.

Methods:
Segmentation was done using multi-dimensional gated recurrent units (MD-GRU; 1,2), a deep learning- based, fully-automated semantic segmentation approach employing a convolutional adaptation of gated recurrent units (GRU; 3). In brief, MD-GRU traverses an image forward and backward along each of its spatial dimensions to infer the current segmentation class label from the local appearance and its surrounding context. The respective neural network was trained for 100'000 iterations on 67 scans (17 HC, 50 patients). Mean Dice score wrt. an expert-labeled manual ground truth was used to select the final training state for evaluation: the state producing the highest score on the 3 labeled sub- regions of the BS (midbrain (M), pons (P) and medulla oblongata (MO)) in a separate set of 20 patients' scans was chosen for further analyses. Expert-labeled manual BS segmentations were then used to validate the accuracy of the automated segmentationin anotherindependent set of 20 patients' scans using Dice scores. The reproducibility of the segmentations was assessed in 11 HC that underwent a MR test-retest experiment with repositioning in-between. The mean %-change betw. test and retest and the respective intra-class correlation coefficients (ICC) were calculated.

Results:
Accuracy: In the validation set, the mean Dice scores comparing automated to the manual segmentations were (mean/SD):0.97/0.006 (total BS); 0.95/0.015 (M); 0.97/0.008 (P); 0.96/0.014 (MO). Reproducibility: The mean %-change/SD between test-retest scans was 0.47%/0.004 for the automated and 0.82%/0.005 for the manual segmentation of the total BS. The ICC of the automated test-retest segmentations of the total BS, M and P were all > 0.99, of MO 0.97.

Conclusions

Fully automated BS segmentation based on the MD-GRU provides accurate, reproducible segmentations in HC and MS patients in 200sec/scan on a Nvidia GeForce GTX 1080 GPU showing high potential for use in longitudinal studies.

P27
Brainstem atrophy in Multiple Sclerosis quantified by new segmentation method correlates with disability

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Introduction:
Neurodegeneration is the major cause of progressive disability in later stages of Multiple Sclerosis (MS). Atrophy is one of the hallmarks of neurodegeneration in MS that can be assessed by MRI. Brainstem (BS) involvement in MS is regarded as a bad prognostic sign and can, in contrast to most other brain regions affected by MS pathology, limit life expectancy. To date, BS atrophy is not well investigated in MS.

Aims:

1. To investigate BS volumes on high-resolution brain 3D T1-weighted images in patients with MS compared to age- and sex matched healthy controls (HC) using a fully-automated deep learning-based segmentation approach.
2. To assess associations between BS volumes and MS disability.

Methods:
A novel, fully-automated deep learning-based segmentation approach (Andermatt S et al. 2016 (DOI 10.1007/978-3-319-46976-8_15); Abstract: Sander L et al.: Fast and fully-automated, deep learning- based brainstem segmentation method provides accurate and reliable brainstem segmentation in Multiple Sclerosis), was used to assess BS atrophy in 189 patients with diagnosis of MS or CIS according to McDonald criteria 2001 (mean age: 43.5 years, SD 11.0, 133 women, median EDSS 3.0, IQR 2, range 0-7.5, mean disease duration 12.4 years, SD 8.9) and 34 age- and sex-matched HC (mean age 43.5 years, SD 12.1, 23 women). Investigations were performed as part of an ongoing MS cohort-study and included determination of the Expanded Disability Status Score (EDSS).

Results:
Compared to HC, patients showed significant reductions in total BS volumes (% difference: 7.2%, $p = 0.0015$), midbrain (% difference: 6.6%, $p = 0.0007$), pons (% difference: 8.2%, $p = 0.0018$) and medulla oblongata volumes (% difference: 4.7%, $p = 0.0315$). Both relapsing and progressive MS subgroups had significant reduced BS and BS substructure volumes compared to HC. In multivariable regression analysis co-varying for age, sex and disease course, BS volume was significantly associated with EDSS (adj $R2 = 0.33$).

Conclusions:
The novel, fast and fully automated MD-GRU based segmentation method allows for efficient volumetry of the BS and its substructures. MS patients show significant atrophy of the BS and its substructures compared to age- and sex matched HCs. BS volumes correlate with disability in MS. Further longitudinal studies are necessary to investigate the prognostic significance of BS atrophy in MS.

P28
Efficacy of Cladribine Tablets in patients with highly active relapsing-remitting multiple sclerosis: analysis of pooled double-blind data from the CLARITY and ONWARD studies

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Aims:
Patients with relapsing MS (RMS) who show an increased rate of relapse or disability worsening can be described as showing high disease activity (HDA). Treatment with Cladribine Tablets in the CLARITY study, and with Cladribine Tablets added to interferon-β in the ONWARD study demonstrated efficacy vs. placebo (PBO) across a range of patients with active MS. Combining double-blind data from these studies allows assessment of the efficacy of treatment with Cladribine Tablets 3.5mg/kg (cumulative dose). The objective of this post-hoc analysis is to compare the effects of Cladribine Tablets 3.5 mg/kg vs. PBO on the proportion of patients achieving no evidence of disease activity (NEDA) status in HDA subgroups identified using two

sets of criteria in a pooled cohort of patients from CLARITY and ONWARD.

Methods:
Patients from CLARITY and ONWARD were retrospectively stratified using 2 sets of HDA criteria based on relapse history, prior treatment, and MRI characteristics: high relapse activity (HRA; N = 314) and HRA plus disease-activity-on-treatment (HRA+DAT; N = 459). Patients treated with Cladribine Tablets 3.5 mg/kg or PBO who fulfilled these criteria and achieved NEDA were compared over 2 years using odds ratios (ORs) and 95% CIs.

Results:
In the HRA subgroup, 76.5% of Cladribine Tablets 3.5 mg/kg-treated patients were relapse-free, 86.7% were T1 Gd+ lesion-free vs. 50.7% and 35.8%, respectively, for PBO. In the HRA+DAT subgroup, 77.6% were relapse-free and 88.8% were T1 Gd+ lesion-free with Cladribine Tablets 3.5 mg/kg vs. 53.9% and 40.8%, respectively for PBO. In the HRA and HRA+DAT subgroups, 42.7% and 41.3%, respectively, of Cladribine Tablets 3.5 mg/kg-treated patients were disease activity free compared with 9.7%, (OR 6.94; 95% CI: 3.67, 13.12; $p < 0.0001$) and 13.7% (OR 4.28; 95% CI: 2.62, 6.99; $p < 0.0001$) respectively, of PBO recipients. In the overall CLARITY+ONWARD population (including non-HDA patients), the composite NEDA score also favoured Cladribine Tablets over PBO (OR 3.95; 95% CI: 2.90, 5.37; $p < 0.0001$).

Conclusions:
Compared with placebo, treatment with Cladribine Tablets 3.5 mg/kg was associated with increased odds of achieving NEDA in HDA patients.

P29
Long-term lymphocyte counts in patients with RRMS treated with cladribine tablets

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Aims:
Cladribine Tablets efficacy was demonstrated in the CLARITY study. Lymphopenia was the most commonly reported AE, consistent with Cladribine Tablets' mechanism of action. Absolute lymphocyte counts (ALC) were investigated to 312 weeks and B and T cell subsets to 240 weeks after the first administered Cladribine Tablets dose, in patients with RRMS receiving 2 annual courses of Cladribine Tablets (3.5mg/kg cumulative dose) followed by no further active treatment.

Methods:
Data from patients randomised to Cladribine Tablets in CLARITY/CLARITY Extension including time in the PREMIERE registry (N = 685) were pooled. Median cell counts are reported.

Results:
Baseline ALC was 1.86 × 109/L. During Year (Y)1, ALC reached nadir at Week (Wk) 9 (1.00 × 109/L) and then gradually increased. During Y2, ALC reached nadir at Wk55 (0.81 × 109/L), recovered to normal (≥ 1.00 × 109/L) by the end of Y2 (Wk96), continuing to increase thereafter. ALC returned to normal in 75% of patients by Wk144. Baseline CD4+ was 851 cells/μL. After treatment in Y1, CD4+ reached nadir at Wk16 (385 cells/μL) and then gradually increased. CD4+ reached nadir after Y2 treatment at Wk60 (292 cells/μL). Values reached the 350 cells/μL threshold by approximately Wk120, continuing to improve thereafter. Baseline CD8+ was 378 cells/μL. CD8+ reached Y1 nadir at Wk16 (239 cells/μL), then gradually increased; Y2 nadir was reached at Wk72 (232 cells/μL). CD8+ recovered quickly after treatment and never dropped below the 200 cells/μL threshold. Baseline CD19+ was 205 cells/μL. After Y1 treatment, CD19+ reached nadir at Wk9 (18 cells/μL) and after Y2 treatment at Wk52 (31 cells/μL). CD19+ then gradually recovered, reaching the 100 cells/μL threshold by Wk96, continuing to improve thereafter.

Conclusion:
Lymphocyte recovery begins soon after Cladribine Tablets treatment, with ALC, CD19+ B cells and CD4+ T cells reaching threshold values by 7.5, 12 and 18 months, respectively, after the last dose in Y2. CD8+ cells never dropped below the threshold.

P30
Cladribine Tablets produce selective and discontinuous reduction of B and T lymphocytes and NK cells in patients with early and relapsing MS

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Aims:
Efficacy of Cladribine Tablets was demonstrated in patients with early MS (ORACLE-MS) and RRMS (CLARITY/Extension). We evaluate the effect on B, T and NK cell profiles after Cladribine Tablets administration.

Methods:
Longitudinal evaluation of peripheral blood lymphocyte subtypes was conducted for patients receiving the first course of Cladribine Tablets either from the initial 3.5mg/kg active treatment groups (ORACLE- MS and CLARITY) or the placebo-switched-to-active-treatment groups (CLARITY Extension). Lymphocytes were immunophenotyped at baseline, and Weeks 5, 13, 24 and 48. Changes in cell numbers and composition of lymphocyte subtypes were evaluated.

Results:
Temporal profiles of CD19+ B lymphocytes and CD4+ and CD8+ T lymphocytes were generally consistent across studies. The fastest cell reduction occurred with CD19+ B cells (approximately 75% at Week 5 in each study). CD19+ B cell nadir occurred at Week 13 with 81%, 84% and 82% median reductions for patients recieving Cladribine Tablets in CLARITY (N = 97), CLARITY Extension (N = 136), and ORACLE-MS (N = 41). Reconstitution of CD19+ B cells towards baseline occurred from Week 24–48. CD4+ and CD8+ T cells were also markedly reduced, but less than CD19+ B cells (at most 55% at Week 13 for CD4+ cells and 48% at Week 48 for CD8+ cells in patients treated with Cladribine Tablets in ORACLE-MS). Reductions in T cells were discontinuous but had not fully returned to baseline by Week 48. CD16+/CD56+ NK cells were also transiently reduced; nadir occurred at Week 13 in ORACLE- MS (44% reduction), with recovery at Weeks 24 (29% reduction) and 48 (23% reduction).

Conclusions:
Cladribine Tablets achieved an early and discontinuous reduction of B cells with rapid reconstitution to baseline, and a moderate and discontinuous reduction in T cells. There were early decreases in NK cells followed by rapid recovery.

P31
If a family forgets – a familiar transient global amnesia in an Italian family

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Introduction:
The transient global amnesia (TGA) is a disease characterized by a short-term memory disorder that lasts for up to 24 hours and is accompanied by disorientation in time, situation and location. Typically, patients are appearing confused and ask repetitive same questions. The cause of this disease is not yet fully understood. MRI often shows hyperintense lesions in diffusion-weighted imaging in the area of the hippocampus. Circulatory disorders as well as migraine or epilepsy-associated phenomena are discussed. For the duration of the symptoms, there is a memory gap, while they can remember the period before and after the incident. Structural changes do not occur. Recurrences are rare, but possible. In the following, we would like to introduce 2 affected brothers (both doctors) and the mother developed a TGA. A brother even experienced a recurrence.

Case:
The 60-year-old patient D.E. was present in February 2018 to clarify a TGA in a neurological consultation in our hospital. The patient had a sudden loss of memory on February 04th, 2018 while visiting a hockey game. He could not remember the time between the beginning and the end of the game.

No neurological deficits were detectable in the clinical examination and the EEG did not show typical epilepsy potentials. An MRI revealed a diffusion disorder in the left hippocampus, which is characteristic for TGA. Also the patient's brother, P.E., a general practitioner, had an episode of sudden memory loss for 30 minutes on May 29th, 2000, while sitting on his sofa. He should have been to work at this point. In his Office, he could not remember that he had emergency duty the previous day and what surgery he had performed on his first patient in the previous week. The following EEG and duplex ultrasound showed no abnormalities. It was noticeable that the patient already had an episode of an ophthalmic migraine, a condition frequently associated with transient global amnesia in the literature. In February 2018 P.E. had another episode of TGA. He had been on vacation with his wife, when he was looking for a toilet. He has no further memory for this time period. The wife reported that he repeatedly asked the same questions. The mother also had a TGA in December 93. A neurological consultation including a CT of the brain and an EEG was without pathological findings.

Conclusion:
We are describing a rare case of a familiar transient global amnesia with one case of recurrent TGA in three family members.

P32
Efficacy and safety of erenumab in episodic migraine patients with 2–4 prior preventive treatment failures: Results from the Phase 3b LIBERTY study

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Objective:
To assess the efficacy and safety of erenumab in patients with episodic migraine who have failed 2–4 prior preventive migraine treatments (PMTs).

Background:
Erenumab is a fully human monoclonal antibody that inhibits the canonical CGRP receptor. Clinical studies have demonstrated the efficacy and safety of erenumab in patients with episodic and chronic migraine. Current oral preventive therapies are associated with low adherence rates due to the lack of efficacy and/or poor tolerability. It is therefore important to assess the safety and efficacy of erenumab in patients who have failed multiple therapies.

Design/Methods:
LIBERTY (NCT03096834) was a 12-week, double-blind, randomized study. Patients (N=246) were randomized (1:1) to receive erenumab 140 mg and placebo. The primary endpoint was the proportion of patients achieving $\geq$50% reduction in mean monthly migraine days (MMDs) during Weeks 9-12 (Month 3). Secondary endpoints included change from baseline to Month 3 in MMDs and monthly acute migraine-specific medication days (MSMDs) and safety/tolerability.

Results:
At baseline, proportion of patients who failed 2, 3, and 4 prior PMTs were 38.6%, 37.8%, and 22.8%, respectively. The mean (SD) MMDs and MSMDs were 9.3 (2.64) and 4.6 (2.89), respectively. At week 12, the proportion of patients achieving $\geq$ 50% reduction in MMD was higher in those treated with erenumab 140 mg vs placebo (30.3% vs 13.7%; OR [95% CI]: 2.73 [1.43, 5.19]; p=0.002). At week 12, there were greater reductions in MMDs and MSMDs with erenumab 140 mg vs placebo (mean difference [95% CI] in MMD: −1.61 [−2.70, −0.52]; p=0.004; mean difference (95% CI) in MSMD: −1.73 [−2.46, −1.01]; p < 0.001). Safety and tolerability profile of erenumab was comparable to placebo. No patients in the erenumab group discontinued due to adverse events.

Conclusions:
These results confirm the efficacy and safety of erenumab in this first dedicated study of a difficult to treat population with 2–4 prior preventive migraine treatment failures.

P33
Treatment satisfaction, quality of life and fatigue in teriflunomide-treated patients in the real-world setting in Switzerland: The Teri-EASY study design

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Aims:
The aim of this presentation is to describe the study design for Teri-EASY, a trial investigating treatment satisfaction, quality of life (QoL), and fatigue in patients with relapsing-remitting MS (RRMS) receiving once daily oral teriflunomide in routine clinical practice in Switzerland.

Methods:
Teri-EASY is an open-label, prospective, non-interventional study conducted at approximately 30 centres in Switzerland. Office-based physicians are responsible for recruiting patients into the study. Planned enrolment is 100 patients. Eligible patients are $\geq$ 18 years of age with a diagnosis of RRMS who initiated treatment with teriflunomide 14 mg, according to the approved Swiss label, as their first MS disease modifying therapy (DMT) or who switched to teriflunomide 14 mg from any other MS DMT. Clinic visits are expected to take place at baseline and at Months 6 and 12. The primary endpoint is change from baseline in patient-reported treatment satisfaction assessed using the Treatment Satisfaction Questionnaire for Medication (TSQM, Version 1.4) questionnaire at Month 12. Secondary endpoints include change in TSQM from baseline to Month 6; change in QoL assessed using the Multiple Sclerosis Quality of Life 54 Instrument (MSQoL54) from baseline to Months 6 and 12; change in fatigue assessed using the Modified Fatigue Impact Scale (MFIS) from baseline to Months 6 and 12; and change in disability assessed using the Expanded Disability Status Scale from baseline to Months 6 and 12.

Results:
The Teri-EASY study will begin recruitment later in 2018.

Conclusion:
Teri-EASY is expected to provide valuable information about treatment satisfaction, QoL, and fatigue outcomes in teriflunomide-treated patients with RRMS in the real-world setting in Switzerland. If you are interested in taking part in the study please contact one of the authors. Study supported by Sanofi.

P34
Next generation sequencing is a promising tool for the diagnosis of hereditary neuropathies

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Introduction:
Hereditary neuropathies constitute a large group of mendelian disorders with varied clinical presentations including notably Charcot-Marie-Tooth (CMT) disease, hereditary sensory and autonomic neuropathy (HSAN) and neuropathies associated with generalized disorders. Next Generation Sequencing (NGS) challenges established hereditary neuropathy classification by revealing that a defined clinical presentation may be due to a large number of genetically distinct subtypes. Here we present our experience with NGS applied to patients with suspicion of hereditary neuropathy after exclusion of CMT1a, Friedreich's ataxia, mitochondrial disorders, neurofibromatosis type 1, and familial amyloid polyneuropathies.

Methods:
Targeted NGS analysis in the form of validated and customized "gene panels" (e.g. neuropathy panel) has been performed in 13 patients seen between 2016 and 2018. The first step consisted of a comprehensive evaluation of personal and family history, clinical findings, and existing laboratory data in the frame of a joint clinical meeting between a neurologist, a metabolic disease specialist and a geneticist together with biologists. Following molecular analysis, this group of experts interpreted the variants identified.

Results:
Pathogenic genetic variants explaining the clinical presentations were identified in 7 patients while 6 cases remained unexplained. One example of a resolved case is provided here, namely, of a 65 year- old woman with a spastic gait since childhood who progressively developed a motor neuropathy with bilateral foot drop and a pigmentary retinopathy. The finding of a homozygous missense mutation c.1580G>A (p.Arg527Gln) in the DDHD1 gene confirmed the diagnosis of hereditary spastic paraplegia of type 28.

Conclusions:
NGS appears to be a promising tool for the diagnostic workup of patients with suspected hereditary neuropathies. In our experience, gene panel testing resulted in several interesting results and a causative mutation was found in more than half of the patients.

P35
Ozanimod (RPC1063) reduces plasma levels of neurofilament light chain in patients with relapsing multiple sclerosis: Results from RADIANCE Part A, a randomized, placebo-controlled, phase 2 study

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Aim:
Ozanimod, a once-daily, oral immunomodulator that selectively targets sphingosine 1-phosphate receptor 1 (S1P1) and 5 (S1P5), has shown therapeutic benefit in relapsing multiple sclerosis (RMS) clinical studies. Modulation of S1P1 on lymphocytes may disrupt the inflammatory cascade of MS. Neurofilament light chain (NfL), which is released into cerebrospinal fluid and serum/plasma following neuroaxonal injury, may serve as a putative biomarker for neurologic damage. This study aimed to evaluate plasma NfL levels in patients with RMS participating in the RADIANCE phase 2 study.

Methods:
In RADIANCE phase 2 (NCT01628393), patients with RMS were randomized (1:1:1) to once-daily oral ozanimod HCl 1.0 or 0.5 mg (equivalent to ozanimod 0.92 and 0.46 mg, respectively) or placebo for 24 weeks. The primary endpoint was mean cumulative number of gadolinium-enhancing lesions from weeks 12–24. Mean cumulative number of new/enlarging T2 lesions from weeks 12–24 was a secondary endpoint. Plasma NfL was measured at baseline and week 24 using Simoa technology.

Results:
At baseline, median plasma NfL was 12.33, 12.33, and 11.69 pg/mL for ozanimod HCl 1.0 mg ($n = 83$), ozanimod HCl 0.5 mg ($n = 87$), and placebo ($n = 88$), respectively. Higher baseline NfL was associated with greater baseline gadolinium-enhancing lesion counts and T2 lesion volume. Median plasma NfL at week 24 was 9.28, 9.39, and 11.77 pg/mL, respectively. The decrease in NfL levels from baseline to week 24 differed significantly for ozanimod HCl 1.0 mg ($p = 0.0087$) and 0.5 mg ($p = 0.0048$) vs placebo. Relative to placebo, treatment with both ozanimod doses reduced the mean cumulative numbers of gadolinium-enhancing (both $p < 0.0001$) and new/enlarging T2 lesions (both $p < 0.0001$).

Conclusion:
Treatment with both ozanimod doses significantly reduced NfL levels between baseline and week 24 by 25% vs placebo. These declines may correlate with the clinically significant reductions in new gadolinium-enhancing and new/enlarging T2 lesion development over weeks 12–24 seen with ozanimod treatment. These data suggest that plasma NfL is a potential biomarker of brain lesion activity, but additional studies are needed.

P36
Patient-Reported and Clinical Outcomes in Teriflunomide-Treated Patients with Relapsing Remitting Multiple Sclerosis: Results from the Real-World TACO Study

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Aims:
Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing forms of MS. TACO is a Phase 4 real-world study conducted to characterize patient-reported outcomes (PROs) and clinical outcomes in patients with relapsing-remitting MS (RRMS) receiving teriflunomide in Switzerland. TACO study design, baseline characteristics, and final core study results will be presented.

Methods:
TACO is an ongoing prospective, non-interventional, single-arm, open-label study conducted across nine sites in Switzerland. Eligible patients had a diagnosis of RRMS according to McDonald 2010 criteria and decided to start treatment with teriflunomide 14 mg once daily independent of study entry and according to local prescribing information. Clinical visits are scheduled at baseline and every 6 months up to 24 months. The primary endpoint is quality of life (QoL), measured using the Multiple Sclerosis Impact Scale-29 (MSIS-29). Secondary endpoints include other PROs (fatigue, depression, cognition, and treatment satisfaction), clinical efficacy (number of relapses and disability worsening), safety and tolerability, and health economics outcomes (medical consultations, in-patient days, and work/school absence). TACO is ongoing; the estimated date of completion of the core study is June 2018.

Results:
The results of the core study will be presented at the meeting. This comprises the data of 57 patients that have been enrolled. The majority (n = 35; 61.4%) are female. At baseline, the mean age was 49.3 years (standard deviation [SD] = 12.2), mean (SD) time since diagnosis was 11.5 (10.0) years, and mean (SD)/median (range) baseline Expanded Disability Status Scale (EDSS) score was 2.4 (1.1)/2.5 (0 to 7.5). A total of 42 (73.7%) patients had received at least one prior disease modifying therapy.

Conclusion:
The real-world, non-interventional TACO study will provide valuable information on clinical and patient-reported outcomes in teriflunomide-treated patients with RRMS in Switzerland. Final core results will be presented. Study supported by Sanofi.

P37
Brain MRI Activity and Atrophy Measures in Patients Receiving Continuous Ocrelizumab or Switching From Interferon ß-1a to Ocrelizumab in the Open-Label Extension Period of the Phase III Trials of Ocrelizumab in Patients With Relapsing Multiple Sclerosis

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Background:
The efficacy and safety of ocrelizumab (OCR) in relapsing multiple sclerosis (RMS) were demonstrated in the 96-week double-blind control period of OPERA I and II (NCT01247324; NCT01412333).

Aim:
To assess the efficacy of switching to or maintaining OCR therapy on MRI measures of disease activity and progression in the open-label extension (OLE) period of Phase III trials in RMS.

Methods:
At the start of the OLE period, patients continued (OCR-OCR) or were switched from interferon-beta-1a (IFNβ1a) to OCR (IFN-OCR). Magnetic resonance imaging (MRI) lesion activity (T1 gadolinium-enhancing [T1Gd+] lesions, new/enlarging T2 [N/ET2] lesions) and percentage change in whole brain volume (WBV), cortical grey matter volume (cGMV) and white matter volume (WMV) were analyzed.

Results:
Among IFN-OCR patients, adjusted number of T1Gd+ lesions was 0.48 lesions/scan at time pre-switch, and decreased to 0.00 at Years 1 and 2 of OLE; similar reductions in adjusted number of N/ET2 lesions were seen from 2.16 lesions/scan in the pre-switch year to 0.33 and 0.08 at Years 1 and 2 of OLE. OCR- OCR continuers maintained low numbers of T1Gd+ and N/ET2 lesions through 2 years of OLE. OCR- OCR continuers versus IFN-OCR switchers

had lower brain atrophy from core study baseline to the end of Years 1 and 2 of the OLE period measured by WBV change (–1.31%/–1.51% and –1.57%/–1.88%; $p < 0.01$ for both), cGMV change (–1.47%/–1.56% and –1.72%/–1.91%; $p = 0.16$ and $p < 0.01$) and WMV change (–0.94%/–1.23% and –1.11%/–1.46%; $p < 0.01$ for both).

Conclusions:
Switching from IFNβ1a to OCR at the start of the OLE period was associated with rapid and robust reductions in MRI disease activity. Patients initially randomized to OCR maintained lower tissue loss in whole brain, white matter and cortical grey matter after 4 years of continuous treatment compared to those initiating OCR 2 years later.

P38
Effect of Teriflunomide on Greater Disability Worsening in Patients With Relapsing Forms of MS in a Pooled Analysis of the Phase 3 TEMSO and TOWER Studies

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Aims:
To assess the effect of teriflunomide 14 mg on greater disability worsening using 3 exploratory definitions of 12-week confirmed disability worsening (12wCDW), in a post hoc analysis of the pooled TEMSO/TOWER dataset.

Methods:
In TEMSO and TOWER, 12wCDW, defined as a $\geq$1.0-point increase in Expanded Disease Severity Status Scale (EDSS) score from baseline ($\geq$0.5 point when baseline was >5.5), was a key secondary endpoint. We assessed 12wCDW using both the original definition (OD) and the following exploratory definitions: D1: $\geq$1.5 points (baseline $\leq$5.5) or $\geq$0.5 point (baseline >5.5); D2: $\geq$2.0 points (baseline $\leq$5.5) or $\geq$0.5 point (baseline >5.5); D3: $\geq$2.0 points (baseline $\leq$5.5) or $\geq$1.0 point (baseline >5.5). Risk of 12wCDW was assessed using a Cox proportional hazards model. Analyses were conducted for the full intention-to- treat (ITT) population, and also for patients who stopped treatment with another disease modifying therapy within the 6 months prior to entering the TEMSO or TOWER trial (referred to as 'switchers' hereafter).

Results:
For the pooled ITT TEMSO/TOWER dataset, risk of 12wCDW by OD was reduced for teriflunomide 14 mg (n=728) vs placebo (n=751): hazard ratio (HR) (95% confidence interval [CI]), 0.695 (0.542, 0.892), P=0.0037. The effect of teriflunomide was maintained using higher thresholds of EDSS increase (D1: HR 0.600 [95% CI 0.415, 0.868], P=0.0055; D2 and D3: HR 0.613 [95% CI 0.380, 0.988], P=0.0436). For the switchers dataset, risk of 12wCDW by OD was reduced for teriflunomide 14 mg (n=90) vs placebo (n=86): HR (95% CI), 0.365 (0.187, 0.712), p=0.0047. The effect of teriflunomide was maintained using higher thresholds of EDSS increase (D1: HR 0.176 [95% CI 0.055, 0.568], P=0.0049; D2 and D3: HR 0.159 [95% CI 0.033, 0.756], P=0.0103).

Conclusion:
Teriflunomide significantly reduced the risk of 12wCDW when more-stringent exploratory definitions were used, in both the ITT and switchers populations. These observations are consistent with primary analyses in both studies and provide further insight into the positive impact of teriflunomide on disability worsening in patients with relapsing MS.

P39
Functional impact of apoE on abcg2-specific therapeutic substrates of neuroimmunological diseases

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Background:
Different immunotherapeutics used in Multiple Sclerosis (MS), e.g. teriflunomide (teri), mitoxantrone (MX) and cladribine are known substrates of the ATP-binding cassette (ABC) transporter ABCG2. Hence, modulators of transporter activity could have potential therapeutic implications in MS. Apolipoprotein E (ApoE) modulates transporter activity in experimental stroke, but effects on ABC- transporters in chronic autoimmune neuroinflammatory disease are unknown.

Objective:
To investigate functional impact of apoE on abcg2-specific substrate effects in vitro and in vivo in association with abcg2 modulation.

Methods:
abcg2-mRNA expression (spinal cord, brain, liver, spleen, splenic T cells) from wildtype (wt) and apoE- deficient (apoE-KO)-mice were analyzed by qRT-PCR. Stimulated T cells from wt and apoE-KO mice (anti-CD3, 10 µg / ml + anti-CD28, 10 ng / ml) were treated with teri (100 µM /

DMSO) or MX (1 μM / A. dest.) or respective vehicle. Intracellular concentration was measured by HPLC (teri) or flow cytometry (MX). T cell apoptosis (24 h; annexinV/PI) and proliferation (48 h; CSFE) were analyzed by flow cytometry. Chronic EAE was induced by active immunization with MOG35-55 in wt and apoE-KO mice. MX (0.5 mg / kg) was given i.v. after individual disease onset (d1) for four days (d1-d3 and d5).

Results:
apoE-KO mice exhibited 1.8-fold higher abcg2-mRNA expression specifically in splenic T cells than wt ($p = 0.008$). Whereas abcg2 expresion in the other analysed organs/tissues were similar in both genotypes. Although T cells from apoE-KO mice revealed decreased in vitro effects of teri (difference apoE-KO vs. wt: teri-induced inhibition of proliferation = -1.6-fold, $p = 0.003$; teri-induced apoptosis = -1.3-fold, $p = 0.005$) and MX (difference apoE-KO vs. wt: MX-induced apoptosis = -1.2-fold, $p < 0.001$), no differences were seen in the intracellular concentration. In vivo, MX-treatment ameliorated clinical EAE-course in apoE-KO mice but not in wt controls (MX vs. vehicle, apoE-KO: $p < 0.001$; wt: $p =$ not significant).

Conclusion:
Functional impact of apoE on abcg2-specific substrates teri and MX was indicated by decreased effects in murine T cells in vitro. In contrast, treatment response to MX in vivo was increased in apoE-KO mice compared to wt controls. However, if observed apoE-dependent effects on teri and MX are associated with altered abcg2-mediated drug efflux or rather with efflux-independent mechanisms, is currently under investigation.

40
Pharmacological Manipulation of the Endocannabinoid System in a Preclinical Model of PostTraumatic Stress Disorder

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Aim:
To determine whether modulating the endocannabinoid (EC) system could alter extinction or anxiety- type behaviour in weak-extinction (WE) and strong-extinction (SE) rats.

Background:
Post-traumatic stress disorder (PTSD) is a debilitating illness associated with extinction impairment, long-term fear responses to stress-related cues, and persistent anxiety after a traumatic experience. The EC system has been implicated in the control of fear and anxiety, with preclinical studies suggesting that ECs facilitate fear extinction and produce anxiolytic effects. One of the main EC receptors in the brain is the type 1 cannabinoid receptor (CB1) and fatty acid amide hydrolase (FAAH) is one of the EC- degrading enzymes.

Methods:
Male Sprague-Dawley rats were subjected to a classical fear conditioning paradigm and then segregated into WE and SE groups based on their freezing behaviour. WE rats present several features analogous to PTSD-like states, including impaired extinction of a conditioned fear response and long-term anxiety. In contrast, SE rats display fast rates of extinction. Two weeks following fear conditioning, the rats were subjected to a long-term recall trial and a novelty supressed feeding (NSF) test. Prior to these behavioural tests, the rats received acute intraperitoneal drug injections. URB597 (0.3 mg/kg), a FAAH inhibitor, was injected in WE rats to test whether increasing synaptic EC levels would improve extinction learning and anxiety-type behaviour. AM251 (3.0 mg/kg), a CB1 receptor antagonist, was injected in SE rats to test whether antagonizing EC would impair extinction and induce anxiogenic effects.

Results:
During the long-term recall trial, acute injections of URB597 (0.3 mg/kg) and AM251 (3.0 mg/kg) did not significantly alter freezing behaviour between WE-URB597 (n=8) and WE-VEH (n=7) or SE-AM251 (n=8) and SE-VEH (n=9). For the NSF test, acute drug injections of URB597 (0.3 mg/kg) and AM251 (3.0 mg/kg) did not significantly alter latency to eat between WE-URB597 (n=8) and WE-VEH (n=7) or SE- AM251 (n=8) and SE-VEH (n=9).

Conclusions:
Acute injections of URB597 (0.3 mg/kg) did not improve extinction learning and anxiety-type behaviour in WE rats. Acute injections of AM251 (3.0 mg/kg) did not impair extinction and induce anxiogenic effects in SE rats. The lack of improvement in extinction learning and anxiety for WE rats may be attributed to indirect methods of increasing EC levels or under-dosage.

P41
Unilateral MR guided High Intensity Focused Ultrasound in Parkinson's disease or essential tremor seems to be save concerning Dysphagia and Dysarthria

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Aim & Background:
MR-guided high intensity focussed ultrasound (MRgFUS) allows ablation of deep brain structures without affecting surrounding tissue. Dysphagia and dysarthria following pallidotomy and subthalamotomy have been described in the past but comprehensive swallowing assessments including instrumental testing (Fiberoptic Endoscopic Evaluation of Swallowing, FEES as one of the gold standards are lacking.We aimed to investigate safety regarding swallowing and speech in MRgFUS ablation in patients with movement disorders.

Methods:
Prospective, open label observational study of swallowing and speech after unilateral MRgFUS ablation within the pallidothalamic tract (PTT) or cerebellothalamic tract (CTT) in patients with Parkinson's disease (PD) and Essential tremor (ET). Unilateral ablation of the PTT (in PD patients) or CTT (in ET patients) was done with the ExAblate Neuro MRgFUS system. Swallowing assessment consisted of a comprehensive clinical assessment by the speech and swallowing specialists including instrumental testing (FEES by video recording) before and 6 months after intervention. Dysphagia was graded using the Penetration-Aspiration Scale3 ranging from 1 (no penetration) to 8 (aspiration). Speech intelligibility was graded using the speech intelligibility rating scale4 (SIRS) ranging from 1 (no intelligibility) to 5 (normal intelligibility). Motor symptoms were assessed using the UPDRS III in PD and Fahn Tolosa Marin Score in ET patients pre, post and 1,3 & 6 months after the intervention.

Results:
3 PD (1 m, 65y $\pm$12) and 6 ET patients (2 m, 71y $\pm$ 8) received unilateral MRgFUS ablation. None of the patients reported dysphagia and clinical assessment remained unchanged with an aspiration- penetration score of 1 at baseline and at follow up. Swallowing assessment 24 months after intervention of one patient with bilateral PTT ablation was normal (score 1). Speech intelligibility remained normal (SIRS 1) after treatment in all patients. The PD patient with bilateral treatment progressed from SIRS 3 (baseline) to SIRS 4 (24 months). In PD patients the mean UPDRS III (ON) score improved from 32.5 $\pm$ 12.5 at baseline to 8.7 $\pm$ 4.4 after 6 months. In ET patients, tremor of the treated hand was improved by 84.3%.

Conclusion:
Unilateral MRgFUS ablation of the PTT in PD patients or CCT in ET patients is safe regarding dysphagia and dysarthria and highly effective regarding motor improvement.

P42
Executive functioning does not contribute to locomotion in amyotrophic lateral sclerosis patients

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Objective:
Amyotrophic lateral sclerosis (ALS) is characterized by co-existing motor and cognitive decline. A relationship between locomotion and cognition has been explored in aging and dementia; however, this issue has never been studied in ALS. We hypothesized that impairments in executive functioning could be linked to disturbances of mobility ALS patients.

Methods:
Totally, 49 non-demented ALS patients were evaluated in the Center for ALS and Related Disorders at Geneva University. Exclusion criteria were: inability to complete the procedures, other disease interfering with mobility, diagnosis of frontotemporal dementia, atypical neurological findings. We assessed the executive function and locomotion using the Frontal Assessment Battery (FAB), the Timed Up and Go (TUG), its imagined version (iTUG) and the delta time.

Results:
No correlation was found between the total FAB score and TUG, iTUG and delta time. Patients were divided into 2 subgroups for each of the FAB subtests (FAB subtest score intact or any abnormality). No correlation was found between TUG, iTUG and delta time and any FAB subscore, except for the iTUG and the conflicting instructions score (8.7 ± 5.7 points versus 5.6 ± 2.1 points, $p = 0.01$). There was no correlation between the total FAB score, its subscores and ALSFRS-R score.

Conclusions:
We did not find any association between executive function and locomotion, what is different from aging and other neurodegenerative conditions. This specificity of ALS may suggest that locomotor disability is explained by other factors such as muscle strength or pyramidal symptoms at an early stage of ALS.

P43
Longitudinal Multidisciplinary Follow-up of Patients With Amyotrophic Lateral Sclerosis

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterised by loss of motor neurones in the spinal cord, brainstem, and motor cortex leading to progressive loss of motor functions, causing tetraplegia,

dysphagia and dysphonia, as well as respiratory failure. Only about 20% of patients survive between 5 and 10 years after symptom onset. A multidisciplinary approach has emerged as the optimal care to ALS patients associated with increased survival and enhanced quality of life.

Between June 2012 and September 2016, we enrolled patients with suspected ALS from Canton of Geneva. We collected clinical findings, anthropometric data, pulmonary function tests, nocturnal oximetry and evaluation by occupational therapists and by physiotherapists on a quarterly basis. Nerve conduction studies were done at the beginning of the follow-up. Quality of life was evaluated through the SF-36 score.

52 out of 68 patients (77%) had a clinical definite, probable or possible diagnosis of ALS according to the Revised El Escorial criteria. Mean time from onset of symptoms to diagnosis was 13.7 months $\pm$ 10.2. 13/68 (19%) had a bulbar onset and four patients had frontotemporal dementia. The median ALSFRS-R score at the first visit was 39 (IQR 32-43). 43% of patients needed non-invasive ventilation and 21% a percutaneous endoscopic gastrostomy. Survival rate at 5 years was 56%.

In conclusion, our multidisciplinary approach could have a positive effect on survival rate.

P44
MR-guided high intensity focused ultrasound in Parkinson's disease: A case report with a 5 year follow up

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Objective:
To report a case of a 44 years old male patient suffering from Parkinson's disease for several years. DAT Scan SPECT confirmed the praesynaptic dopaminergic deficit. The patient presented a tremor dominant syndrome resistent to sufficient medical treatment. Deep brain stimulation was no therapeutic option due to comorbidity with former drug abuse. That is why we offered the patient unilateral MR-guided high intensity focused ultrasound (MRgFUS) ablation of the pallido-thalamic- tract (PTT, fasciculus thalamicus) as another therapeutic option.

Background:
MR-guided focused ultrasound (MRgFUS) is a novel technique which allows ablation of deep brain structures under direct MR guidance without affecting surrounding tissue. Lesions and mainly stimulation within the pallido-thalomocortical network (STN, GPi and Vim) are established stereotactic targets to treat parkinsonism. Lesional studies have shown that ablation (radiofrequency, MRgFUS) [1,2] of the PTT within the subthalamic area is an effective approach to treat parkinsonian symptoms like bradykinesia, tremor and rigidity.

Methods:
Retrospective case report out of an ongoing trial. The PD patient fulfilled current criteria for DBS therapy and received unilateral (left) ablation of the PTT using the ExAblate Neuro MRgFUS system. Reason against DBS was malcompliance due to polytoxicomania. The observation period was 5 years. The UPDRS III Score was recorded prior to and 6 months after the intervention. Pre and 6 month post intervention neuropsychological assessments are available.

Results:
The UPDRS III score improved from 23.0 in the best on status prior to the intervention to 15.0 in the best on status 6 months after the intervention lasting up to 5 year follow up. UPDRS III was performed every 6 months. The improvement in UPDRS III is due to complete recovery of contralateral tremor. The Hoehn and Yahr scale did not change after the intervention. No other adverse events were observed.

Conclusions:
This case shows that unilateral MRgFUS of the pallidothalamic tract (PTT) seems to be a safe and effective treatment alternative to DBS for patients with PD especially in tremordominant syndromes. Our patient showed long-term benefit over a 5 year period.