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Epilepsy

SC201

Teratogenesis in repeated pregnancies in antiepileptic drug-treated women

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Introduction: Considerable information exists on risk of teratogenesis in individual pregnancy exposed to antiepileptic drugs (AEDs). Comparatively little is known about risk in subsequent pregnancies for a woman who continues to take an AED that was associated with a foetal malformation in an earlier pregnancy.
Method: Analysis of data concerning foetal abnormalities in 1243 women who had 2637 pregnancies recorded in the Australian Pregnancy Register between mid-1999 and 2010.
Results: Women who had not had malformed foetuses in any previous pregnancy were less likely to become pregnant again if they had taken valproate (VPA) than if they had taken other AEDs (13.0% versus 20.3%; O.R.=1.48; 95% C.I.=1.02, 2.14). Women whose pregnancies had resulted in malformed foetuses, taking VPA were more likely to have further pregnancies with malformed foetuses than women who had taken the drug in pregnancy without foetal abnormalities (57.2% versus 7.0%, O.R.=17.8; 95% C.I.=2.7, 119.1). There were similar trends for other AEDs, but these did not reach statistical significance. If a woman had two or more pregnancies that resulted in AED-associated foetal malformation, the types of malformation were often different.
Conclusions: Women who have had a previous pregnancy resulting in a foetal malformation have a substantially increased risk of having further malformed foetuses if they become pregnant again while taking VPA. This suggests that maternal factors, perhaps genomic, predispose to VPA associated malformations, and should be helpful in advising women with epilepsy who are planning further pregnancies.

SC202

Automatic detection of epileptic seizures with rhythmic and irregular ictal morphology

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Introduction: We propose an improved automatic seizure detection method for long-term EEG recordings that is able to relieve medical staff from continuously monitoring the patient's EEG. Furthermore, a drastical reduction of the EEG evaluation time can be achieved by providing high detection sensitivity with low false alarm rates.
Methods: The online seizure detection method EpiScan published in [1,2] searches for rhythmic ictal patterns in surface EEG recordings typically seen in TLE. Here we enhanced this method for patients having irregular ictal morphology and ictal signal distortions. The method was evaluated on 22,000h of uncut EEG recordings from 275 patients including 96 patients with seizures.
Results: The results improved especially for seizures with irregular ictal morphology. The mean sensitivity was 73% corresponding to an increase of 15% compared to [2] while having 0.3 false alarms per hour (FA/h). More than half of the patients (n=50) had a sensitivity of 100%, 23 patients had a good sensitivity over 50% leaving only 23 patients below 50%. Compared to [2] a 10% increase in sensitivity of eTLE was achieved. TLE showed a sensitivity of 83.6% with 0.29 FA/h.
Conclusion: Automatic seizure detection for surface EEG recordings was presented that reaches high overall detection performance on a statistically relevant EEG database. The detection of irregular ictal morphology improves overall sensitivity.
References:
[1] M. Hartmann, et.al „EpiScan: Online seizure detection for epilepsy monitoring units", IEEE EMBC 2011
[2] F. Fürbaß, et.al. „Detection of Epileptic Seizures During Pre-Surgical Evaluation using Rhytmic EEG Patterns", EFNS 2011

SC203

Interchangeability of gabapentin generic formulations in The Netherlands: a comparative bioavailability study

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Introduction: In order to investigate the possible "drifting effect" upon generic-generic exchange, a comparative bioavailability trial was conducted in healthy volunteers with four formulations of gabapentin registered in The Netherlands.
Methods: This study was designed as a single dose, four-treatment, randomised, four-way crossover trial in 24 healthy volunteers under fasting conditions. Neurontin® or one of three registered generic gabapentin products were administered at a dose of 800mg, and the drug exposures over 48 hours was studied. Gabapentin plasma levels were determined using a validated LC-MS/MS method. The 90% CI for the reference/test exposure ratio of ln-transformed gabapentin pharmacokinetic parameters was calculated using ANOVA.
Results: Six comparisons were performed among the four treatments to investigate the bioequivalence of different gabapentin formulations. In all comparisons, the 90% CIs for the reference/test ratio of Cmax, AUCt and AUCinf were within 80.00-125.00% criterion. The safety profiles of volunteers were acceptable.
Discussion: Results are in line with those obtained from a previously conducted simulation study with topiramate and gabapentin based on bioequivalence data present in the registration files of the Dutch Medicines Evaluation Board. Compared with the simulation study for generic-generic interchange, the ratios in the currently reported comparative bioavailability study are comparable, albeit with narrower 90% CIs for Cmax and AUCt.
Conclusion: In this comparative bioavailability study, all three generic formulations of gabapentin were found to be interchangeable with Neurontin®, and were also shown to be bioequivalent to each other. These results indicate the absence of a "drifting" problem upon gabapentin generic-generic exchange.

SC204

Clinical and electroencephalography characteristics déjà-vu phenomenon in epilepsy

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Background: Déjà-vu (DV) phenomenon is the most common and recognizable derealisation disorder.
Aim: To examine the clinical and diagnostic value of deja vu in epilepsy.
Materials and methods: Study group of 166 persons (average age 25.17±9.19; 63.2% of women). Déjà -vu was compared in two groups: first - healthy people (n=139), second - patients with epilepsy (n=27). Long-time EEG monitoring was performed for all patients of the second group and 5 healthy participants with frequent DV. To evaluate the clinical characteristics of DV we used our own unique questionnaire.
Results: For patients with epilepsy, DV phenomenon occurs in cryptogenic and symptomatic focal epilepsy, it can be combined with virtually all types of seizures, could be aura of a seizure, and self-attack. For the first time there was EEG-pattern of DV phenomenon recorded in epilepsy, that is characterized by the beginning of spike activity in the right temporal lobe and, in some cases (longer duration of phenomenon), ended in slow wave, theta-delta activity in the right hemisphere. EEG-pattern of healthy DV-phenomenon characterized by desynchronization of basical EEG-rhythm. The frequency, DV fear of the onset and emotional colouring are the main clinical characteristics that differentiate DV of healthy patients from DV in epilepsy. The most important diagnostic criterion is the dynamic characteristics of the DV.
Conclusion: We found two types of déjà-vu: "pathological-epileptic", characteristic of patients with epilepsy and equivalent a seizure, "non-pathological-non-epileptic" déjà-vu, which is characterized for healthy people and a psychological phenomenon.

SC205

A community-based epidemiological study of epilepsy in Assiut area, Egypt

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Background: The aim of the study was to estimate the prevalence of different types of epilepsy and their possible risk factors in the region of the Assiut area, Egypt.
Material and Methods: A community-based study with random sampling of 7 districts, involving 6498 inhabitants. Patients were evaluated using a screening questionnaire for epilepsy, and then referred to the hospital to be re-evaluated by a qualified neurologist and with electroencephalography (EEG) and CT.
Results: 75 cases were diagnosed with epilepsy giving an overall crude prevalence rate (CPR) for epilepsy of 12.67/1000 (95% CI: 9.8-15.54). 56 cases (75%) had idiopathic epilepsy (CPR 9.5/1000). Symptomatic epilepsy was recorded in 19 (25%) cases (CPR 3.2/1000). Idiopathic generalized seizures were more common (CPR 6.75/1000) than partial seizures (CPR 2.5/1000). The prevalence rate of partial seizures evolving to secondary generalization was 0.84/1000 while simple partial and complex partial seizures had CPR 1.4/1000 and 0.34/1000, respectively. The CPR of mixed seizures was 0.17/1000. Epilepsy was slightly but not significantly more common among males than females (CPR of 14.4 and 10.9 per 1000 population, respectively). The CPR was higher in rural than urban populations (17.7 /1000, with 95% CI 12.2-23.18 and 9.56 /1000, with 95% CI: 6.39-12.7, respectively) and in the illiterate group than the literate population (12.02/1000, and 9.94/1000, respectively). The highest prevalence rate was recorded in the early and late childhood period (69.78/100,000 and 43.78/100,000, respectively). Prenatal insults and infection represented major causes of symptomatic epilepsy.

SC206

Mortality and factors associated with mortality in people living with convulsive epilepsy in a rural area of Kenya

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Background: Most epilepsy mortality studies from Low and Middle Income Countries (LMIC) are based on small cohorts while some have been conducted in areas with high incidence of epilepsy. Furthermore, there are no studies on risk factors of mortality in people with epilepsy. We measured mortality and identified associated factors in a cohort of people with active convulsive epilepsy (ACE) in a rural area of Kenya.
Methods: People with ACE were identified in a cross-sectional survey and followed up quarterly for three years to collect information on putative risk factors of mortality. We estimated case fatality proportion (CFP), mortality ratios and standardized mortality ratio (SMR). We used Poisson regression analysis to examine the influence of potential risk factors on mortality.
Results: We registered 61 deaths among 754 people with ACE (CFP=8.1%). Mortality rate was 33.3/100,000/year (95% CI: 25.9-42.8). The SMR was 6.5 (95% CI: 5.0-8.3) and ACE mortality was higher in all age groups. Non-adherence to treatment was associated with mortality in this population; adjusted Odds Ratio was 4.7 (95% CI: 2.2-10.4).
Conclusion: Epilepsy confers an additional risk of mortality in this population and is associated with non-adherence to treatment which is amenable to public health intervention.

Autonomic nervous system disorders

SC207

Dynamic evaluation of postganglionic sudomotor activity (DEPSA)

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Introduction: Dynamic evaluation of postganglionic sudomotor activity can contribute to the diagnosis of several autonomic disorders. Current methods used to evaluate postganglionic function are quite expensive. We hypothesize that computerized video analysis is a natural choice for low cost sweat evaluation.
Methods: Sweating has been stimulated by iontophoresis of pilocarpine (0.5%, 1.5mA, 10 min). After the ionthophoresis we recorded a 10 minutes video of the progress of a topical pH indicator dye on the region of interest. The frames were converted to an appropriate specific colour space. Movements of the patient and lighting variations were corrected, and thresholds to get sudomotor response information were applied. Finally, we quantified the percent of the stimulated area affected by sweating.
Results: We tested sudomotor function in the forearms of 40 patients; 10 were hyperhidrotic, 15 normohidrotic and 15 hypohidrotic. The response of hyperhidrotic patients reached around the 70% of the sweat production area, showing a sigmoid pattern with high slope. In normohidrotic subjects, final percentages were similar, but the slope was nearly constant in the course of the test. The response of hypohidrotic patients hardly reached a 5%. Sweat response, measured with our system, was consistent with the results seen by other testing techniques.
[Regular patterns of sweating responses]
Conclusions: Sweat response can be assessed with spatial and temporal resolution using digital video processing. We have developed a simple and inexpensive tool for the evaluation of postganglionic sudomotor function that can be easily used for autonomic diagnosis.

SC208

Postictal generalized EEG suppression (PGES) is more frequent in convulsive seizures arising from sleep

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Purpose: Postictal generalized EEG suppression (PGES) seems to be a pathophysiological hallmark in the ictal recordings of sudden unexpected death in epilepsy (SUDEP). It has recently been suggested that the presence and duration of PGES might be predictors of SUDEP risk. Little is still known about its aetiology.
Methods: A retrospective case-control study was conducted in 50 people with convulsive seizures (CS) registered on digital video-EEG. Per individual one CS was reviewed for the presence and duration of PGES by two independent assessors: 37 (74%) patients showed PGES and 13 (26%) did not. Pre- and postictal heart rate (HR) and frequency domain measures of heart rate variability (HRV) including the ratio of low versus high frequency power were analyzed. The relation between PGES and peri-ictal autonomic changes was evaluated, as well as its association with several clinical variables.
Results: PGES was neither associated with peri-ictal HR (mean HR difference between PGES+ and PGES- seizures: -5 bpm, 95% CI -13 to +3 bpm) nor HRV change. There was no relation between duration of the tonic-clonic phase of the seizure and PGES. Patients with PGES were more likely to be asleep prior to seizure onset (OR 4.7, 95% CI 1.2-18.3) and had a higher age of onset (median age; 15 vs. 5 years).
Conclusion: PGES was not associated with substantial changes in measures of cardiac autonomic instability but more prevalent in CS arising from sleep. PGES might be an expression of excessive neuronal inhibition acting as a seizure termination mechanism.

SC209

The effects of the somatostatin analogue, octreotide, on orthostasis before and after food ingestion, in the postural tachycardia syndrome

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Postural Tachycardia Syndrome (PoTS) is characterized by an orthostatic increase in heart rate of ≥30 beats/min without hypotension and symptoms of orthostatic intolerance (OI). The somatostatin analogue, octreotide, reduces orthostatic hypotension and intolerance in other autonomic disorders, but its effects in PoTS are unknown.

Aim: To evaluate the effects of octreotide on orthostasis, before and after food ingestion, in PoTS.

Method: 19 female PoTS patients who had not responded to previous treatment, including non-pharmacological measures, midodrine, fludrocortisone and beta blockers, both alone and in combination, underwent a liquid meal test with and without a sub-cutaneous injection of octreotide (50 mcg). Head-up tilting at 60° (HUT; 9 min or less if OI occurred) was performed pre- and post-meal, and symptoms were recorded. Blood pressure and heart rate were measured using upper arm auto-sphygmomanometry.

Results: Blood pressure was unchanged but heart rate was reduced after octreotide administration ($P>0.05$ and < 0.05, respectively). There was a post-prandial fall in blood pressure and heart rate increased in both conditions (both $p<0.05$). All patients met the criteria for PoTS during HUT pre- and post-meal without octreotide (increases in heart rate >30 beats/min). The heart rate elevations during HUT pre- and post-meal were significantly reduced during octreotide in all patients but 2 (12±9 and 18±11 beats/min, respectively, $p<0.05$). Blood pressure was well maintained during pre- and post-prandial HUT with and without octreotide. Symptoms of orthostatic intolerance were significantly improved with octreotide. These findings indicate that octreotide reduces orthostatic tachycardia and OI in PoTS.

SC210

Atropine influences pupillary diameter oscillations while carvedilol has no effect on pupillary oscillations

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Introduction: Main frequency ranges of sympathetic and parasympathetic pupillary diameter (PD) oscillations are not yet defined while autonomic fluctuations of heart rate (HR) and blood pressure (BP) are associated with spectral powers in the so-called low- (LF: 0.03-0.15Hz) and high-frequency (HF: 0.15-0.5Hz) ranges.

Therefore, we determined by pharmacologic blockade whether PD-oscillations in the LF- and HF-ranges are associated with sympathetic or parasympathetic activity.

Methods: In 13 healthy persons (25±2 years), we recorded HR, BP, and PD by means of infrared-pupillography under resting conditions, after parasympathetic blockade using intravenous Atropine (0.04mg/kg), and again 2-3 hours after alpha-beta-adrenoreceptor-blockade by oral Carvedilol (25mg). We determined normalized spectral powers of HR-, BP-, and PD-oscillations in the LF- and HF-ranges {LFnu= [LF/(LF+HF)]x100%, and HFnu= [HF/(LF+HF)]x100%} and compared powers with and without pharmacologic blockade (ANOVA, post-hoc analysis; significance: $p<0.05$).

Results: Atropine significantly increased HR, LFnu-HR, PD (5.1±1.4 vs. 6.3±1.1mm), and LFnu-PD (38.9±11.6 vs. 59.0±8.2%), decreased HFnu-HR and HFnu-PD (61.1±11.6 vs. 40.9±8.2%), but did not change BP, LFnu-BP and HFnu-BP.

Carvedilol significantly decreased HR and LFnu-BP, insignificantly decreased BP, but did not change LFnu-HR, HFnu-HR, PD, LFnu-PD and HFnu-PD.

Conclusion: Atropine had similar effects on HR and PD, and similarly increased LF- and attenuated HF-oscillations of both signals. Thus, HF-oscillations of PD reflect parasympathetic modulation.

Lack of Carvedilol effects on PD and PD-oscillations might reflect insufficient dosage or inadequate effects on pupillary muscles or indicate that sympathetic PD modulation has its main frequencies not within the LF-range.

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SC211

Autonomic failure exploration: arterial stiffness is correlated to impairment in cardiovascular response

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Primary or secondary autonomic failure (AF) affects patient's quality of life and is a risk factor for cardiovascular morbidity and mortality. Abnormal arterial stiffness has been poorly reported in patients with orthostatic hypotension. The aim of our study was to evaluate the relationship between AF and artery compliance assessed by pulse wave velocity (PWV) and central blood pressure (CBP). 63 consecutive patients referred to the Toulouse University Hospital underwent autonomic testing based on changes on heart rate and blood pressure during Ewing tests. Severity of AF was quantified using Ewing. PWV and CBP were assessed by artery aplanation tonometry. Based on autonomic testing, 34 patients suffered from significant AF (Ewing score>1) whereas 29 patients were devoided of AF (Ewing score≤1). Age, sex and BMI were not significantly different between groups. However, we find more diabetic patients in AF+ group than in AF- (72% vs. 48%) and a majority of not identified etiology in AF- group than in group AF+ (48% vs. 6%). AF+ patients had a significantly higher PWV when compared to AF- group (8.9±0.4 vs. 10.1±0.5 m/s; p=0.016). PWV was significantly correlated to Valsalva ratio (r^2=0.1075; p=0.0136) and to changes in heart rate during deep breathing (r^2=0.2236, p=0.0002). PWV was also correlated to 30/15 ratio (r^2=0.1753, p=0.0009). We show for the first time a direct relationship between PWV and cardiovascular autonomic dysfunction. These results suggest that arterial stiffness could account for abnormal responses during standard autonomic testing and that its assessment should be systematically achieved in AF patients.

SC212

Transcranial direct current stimulation (TDCS) can modulate oesophageal motility in gastro-oesophageal reflux disease (GERD) patients

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Aims: To evaluate the effects of transcranial direct current stimulation (TDCS) on oesophageal manometric parameters in patients with GERD.

Methods: We studied 40 patients with clinical diagnosis of GERD ("Montreal definition") who previously underwent endoscopy to differentiate erosive reflux disease (ERD) from non-erosive reflux disease (NERD). An oesophageal manometry was performed before and during cortical stimulation with TDCS (1.5 mA) on the right oesophageal motor area. Randomly 20 patients were assigned to anodal stimulation, 20 patients to sham stimulation. Distal waves amplitude and number of pathological waves (distal amplitude <30 mmHg or not propagated distal peristalsis) were measured 3 cm over the lower oesophageal sphincter (LES) after swallowing a water bolus, for ten subsequent times. LES pressure was obtained as well. A 24-hours pH-metry was further performed to rule out functional heartburn. Mean waves amplitude, number of pathological waves and mean basal LES pressure were compared by paired-samples T-test before and during TDCS in both groups of patients.

Results: Mean distal waves amplitude increased significantly (p=0.04) and the number of distal pathological waves decreased significantly (p=0.01) during anodal TDCS, while sham stimulation did not influence any parameter. LES mean pressure was not significantly modified during anodal or sham stimulation in GERD patients. Comparison between groups (NERD vs. ERD) showed that significant changes after TDCS occurred only in the NERD subgroup.

Conclusions: Our data suggest that TDCS can influence cortical control of oesophageal motility and improves pathological motor pattern in NERD patients.

SC213

Attenuated heart rate response is associated with hypocretin deficiency in patients with narcolepsy

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Introduction: To determine whether patients with narcolepsy with and without cataplexy, and with and without hypocretin-1 deficiency have attenuated heart rate response (HRR) to arousals from sleep compared to healthy controls.

Method: We analysed the HRR during various sleep stages with a one-night polysomnography in 67 narcolepsy patients compared with 17 age- and gender-matched healthy controls. The narcolepsy group was subdivided by the presence of ± cataplexy and ± hypocretin-1 deficiency (hypocretin-1 level <129 pg/ml). Cataplexy was present in 46/67 patients and hypocretin-1 deficiency in 38/61 patients.

Results: All narcolepsy patients had a significantly reduced HRR associated with arousals and leg movements ($p<0.05$). HRR associated with arousals was significantly lower in the hypocretin-1 deficiency and cataplexy groups compared with patients with normal hypocretin-1 levels ($p<0.04$) and patients without cataplexy ($p<0.04$). To identify the primary predictors of HRR, this outcome was further analysed in relation to cataplexy and hypocretin-1 deficiency using univariate and multivariate linear regression, controlling for possible biasing factors. Only hypocretin-1 deficiency significantly predicted the HRR associated with arousals in both REM and non-REM in the multivariate model.

Conclusion: Narcolepsy patients reveal an attenuated HRR to arousal from both non-REM and REM sleep. This attenuated HRR is further pronounced in patients with cataplexy and/or hypocretin-1 deficiency. The results show that autonomic dysfunction is part of the narcoleptic phenotype, and that hypocretin-1 deficiency is the primary predictor of this dysfunction. This suggests that the hypocretin system participates in the modulation of cardiovascular function at rest.

Cerebrovascular diseases 2

SC214

Carotid intima-media thickness and normal ranges of urine albumin-to-creatinine ratio in Korean adults: the Namwon study

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Aims: Albuminuria has been reported to be a risk marker of systemic diseases such as atherosclerosis, but the association between normal ranges of urine albumin-to-creatinine ratio (UACR) and carotid atherosclerosis has not been examined with a community-based study. We aimed to report the association between normal ranges of UACR and carotid intima-media thickness in Korean adults.
Methods: We performed a cross-sectional study in adults aged 45 to 74 years who were living in Namwon city, South Korea. Carotid intima-media thickness (IMT) at both-sided common carotid artery were measured and their mean values were used. Normal values of UACR were defined as <30 mg/g and categorized into quintiles: less than 6.50, 6.51-9.79, 9.80-13.49, 13.50-18.89, and more than 18.90. The association between the quintiles of UACR and carotid mean IMT was examined with sex stratification.
Results: In total, 7555 participants (3084 men and 4471 women) with normal UACR were analyzed for the present study. Carotid IMT was positively and independently associated with quintiles of UACR in men and women, adjusting for potential confounders including age, body mass index, and cardiovascular risk factors. Compared to the first quintile, the highest quintile showed an odds ratio of 1.75 (95% confidence intervals, 1.23-2.48) and 1.97 (1.28-3.04) for an increased IMT (>0.9cm) in men and women, respectively.
Conclusion: Normal ranges of UACR was positively and independently associated with carotid IMT in the Korean general population.

SC215

Clevidipine rapidly and safely reduces blood pressure in acute intracerebral haemorrhage; The ACCELERATE trial cover title: clevidipine rapidly and safely reduces BP in ICH

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Background and Purpose: Intracerebral haemorrhage (ICH) causes 10-15% of primary strokes with mortality related to haematoma volume. Blood pressure (BP) reduction may attenuate haematoma expansion. The ACCELERATE trial evaluated intravenous clevidipine for the rapid treatment of hypertension in ICH patients.
Methods: ICH patients with a systolic BP (SBP) >160mm Hg who present within 12 hours of symptoms were prospectively enrolled, treated with open-label clevidipine until SBP ≤160mmHg was achieved and then titrated to keep target SBP between 140 to 160mmHg.
Results: 35 patients with baseline median Glasgow Coma Scale (GCS) score 12, median NIH Stroke Scale (NIHSS) score 14, and mean SBP 186mmHg received clevidipine. Median time to achieve SBP target range was 5.5 minutes. All patients achieved target SBP within 30 minutes; 96.9% achieved target SBP with clevidipine monotherapy. CT scans showed minimal haematoma volume change for the overall population (median change -0.01mL; -2.9%). Mild/moderate hypotension was reported in 3 patients and resolved with dose reduction or drug discontinuation.
Conclusion: Clevidipine monotherapy was effective and safe for rapid BP reduction in this cohort of critically ill ICH patients. Overall, patients showed minimal haematoma expansion with BP reduction.
Clinical Trial Registry Information - http://clinicaltrials.gov/ct2/show/NCT00666328?term=clevidipine&rank=5 Unique Identifier:NCT00666328.

SC216

Prognostic factors for outcomes after mechanical thrombectomy with Solitaire FR device

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Introduction: Endovascular mechanical thrombectomy is an emerging promising therapeutic tool at acute phase of stroke. This study aimed at identifying factors influencing outcomes after thrombectomy with Solitaire FR.
Methods: 45 consecutive patients treated with thrombectomy were retrospectively included. Clinical (age, gender, initial NIH), imaging (occlusion location, DWI and Flair results) and logistical (IV fibrinolysis, delay before first Solitaire deployement, geographic origin) variables were analyzed. A multivariate logistic regression allowed identifying variables influencing the clinical efficacy.
Results: 30 men and 15 women were included, with mean age and initial NIHSS of 57.5 years and 16.6. An MRI was performed for 80.0% of patients, showing severe DWI lesion for 27.8% of patients and associated hypersignal FLAIR for 58.3% of patients. An IV fibrinolysis was performed for 42.2% of patients. Mean delay before recanalization was 299 min for the 32 anterior circulation occlusions and 473 min for the 13 posterior circulation occlusions. Angiographic efficacy was obtained for 93.3% of patients and clinical efficacy at discharge and at 3 months was obtained for 48.9 % and 57.8 % of patients, respectively. Death rate was 17.8%. Independent prognostic factors to predict a good clinical efficacy at discharge were a short delay before recanalization and FLAIR negativity; at 3 months a short delay and patient age. Severity of DWI lesion was an associated prognostic factor.
Conclusions: Three main prognostic factors to predict a good clinical outcome after thrombectomy were: short delay before recanalization, patient age and non-severe DWI lesion.

SC217

Intracranial atherosclerosis in Norway. Preliminary results from the Norwegian intracranial atherosclerosis study

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Introduction: No data about prevalence and natural history of Intracranial Atherosclerosis (ICAS) in Northern Europe are available. In a well-defined community based ischemic stroke population we aimed to investigate
1) the prevalence of symptomatic and asymptomatic ICAS;
2) the risk factors associated with ICAS;
3) and the rate of recurrent stroke in ICAS patients
Methods: In a prospective study, all ischemic stroke or TIA patients were screened for intracranial stenosis (IS) by Transcranial Colour-Coded Sonography (TCCS), MR- and/or CT-Angiography. IS was defined as ICAS if other causes of stenosis were excluded. ICAS was defined symptomatic if the infarct/symptoms were related to the territory of the stenotic artery. Risk factors for cerebrovascular disease were registered on admission. Patients with ICAS were followed-up at 3, 6 and 12 months. Follow-up consisted of clinical and TCCS examination, plus CTA at month 12.
Results: During an 18-month study period, 607 patients had a confirmed ischemic stroke/TIA. IS was found in 54 patients (8.9%). 7 patients presenting IS had a possible/probable cardioembolism, ICAS was therefore diagnosed in 47 patients (7.7%). ICAS was symptomatic in 33 patients (5.4%). Diabetes mellitus was the only risk factor significantly associated with symptomatic ICAS. Among ICAS patients, a new ischemic event occurred in 2 patients (4.3%; 1 stroke/1 TIA).
Conclusion: ICAS is present in ~8% and symptomatic in ~5% of a Norwegian ischemic stroke/TIA population. Diabetes mellitus appears to be the major risk factor for ICAS. ICAS appears to carry a low stroke risk.

SC218

Abstract cancelled

SC219

The contribution of risk factor distribution to living standard associated stroke features in the Budapest districts 8-12 project

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Introduction: The Budapest Districts 8-12 project is a comparative analysis of all acute stroke cases hospitalized for stroke in 2007 in 2 districts in Budapest. District 8 is the least wealthy whereas district 12 is the second most wealthy of the 23 districts of Budapest. We previously found that stroke hits earlier and outcome is worse in the less wealthy district. In this analysis we test if differences in traditional stroke risk factors explain some of these differences.
Methods: Hospitalized stroke cases were identified by the database of the National Health Insurance Fund and postal codes for living address. Case certification was performed by personal visits to the general practitioners. Data on risk factors were entered in an anonymized database.
Results: The rate of non- or non-regularly treated hypertension was 5.6% and 24,2% in the wealthy and the poor districts, respectively ($p<0.001$). Diabetes and alcohol dependence are also more frequent in the poor district (25 vs. 17%, $p=0.04$ and 19% vs. 5%, $p<0.01$). The rate of smokers is higher in the poor district, and the proportion of heavy smokers (smoking over 1 pack per day) is 3.2% in the wealthy whereas 17.1% in the poor district. There was no difference between the 2 districts in the rate of atrial fibrillation ($p=0.5$), and peripheral arterial disease ($p=0.19$).
Conclusions: The uneven distribution of risk factors may have a role on the earlier onset and more severe strokes in the poor compared to the wealthy microregions even within one city.

Headache and pain

SC220

Detoxification in a structured programme is effective for medication-overuse headache

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Introduction: Patients who fail withdrawal are often excluded from studies on medication-overuse headache (MOH). We aimed to evaluate the long-term efficacy of two different MOH treatment programmes in so-called treatment-resistant patients.
Methods: MOH patients, who had previously been unsuccessfully treated by neurologists, were enrolled in one of 2 structured detoxification programmes in a tertiary headache centre: A) a one-week withdrawal with restricted analgesics, rescue medications and prophylactics from day 1 followed by restricted intake of symptomatic medications or B) a 2-month drug-free period and multidisciplinary education in groups and subsequent initiation of restricted symptomatic medication and prophylactics as required. All patients were closely followed up for a year.
Results: 86 of 98 patients completed the 12-month follow-up. Totally, headache frequency was reduced by 39% ($p<0.001$), medication use by 63% ($p<0.001$) and 83% remained cured of MOH. Headache frequency was reduced by ≥50% in 42 patients (49%) and 52 (61%) reverted to episodic headache, and with no difference between the groups. Patients in programme B used significantly less symptomatic medication: 6.5 days/4 weeks compared with 8.7 days/4 weeks in programme A ($p=0.02$), and the 56% of patients in programme B who needed prophylactic medication was significantly less than the 80% in programme A ($p=0.02$). Furthermore, programme B required fewer resources from the staff.
Conclusion: Structured detoxification with close follow-up for one year is highly effective in patients with previously treatment-resistant MOH. We recommend a multidisciplinary educational programme for patients in groups due to cost-effectiveness and limited use of medication.

SC221

Risk factors of migraine - a co-twin control study

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Objective: To evaluate the effects of a variety of diseases and environmental risk factors on the risk of migraine.
Methods: In 2002, more than 30,000 twin individuals participated in a questionnaire survey. Only complete same-sexed twin pairs discordant for migraine were included in this co-twin control study, which comprised 1274 female and 600 male pairs. This design allowed us to control for most shared genetic and environmental predisposition.
Results: Low back pain, neck pain and whiplash were significantly associated with migraine with an increased risk of 50-115%. Arterial hypertension, kidney stone, osteoarthritis and tinnitus were also significantly associated with migraine. Coronary thrombosis and other thrombosis as separate entities were not associated with migraine, however, when pooled together there was a significantly increased risk (OR=1.88[1.14 -3.08], $p=0.01$). Weekly alcohol consumption was the only environmental factor significantly associated with migraine. The risk was decreased with almost 20%. The effect of obesity on the risk of migraine was 1.5, however, this was not statistically significant ($p=0.07$).
Conclusion: This is the first large co-twin study of co-morbidities and environmental risk factors in migraine. A number of co-morbidities were confirmed but no environmental risk factors besides alcohol consumption were significant. Alcohol is a potent inducer of migraine attack therefore the association between alcohol and migraine is likely due to an avoidance reaction towards alcohol. Conventional socio-economic and lifestyle factors therefore do not seem to be important. Further studies should focus on other factors e.g. emotional factors such as stressful events.

SC222

An fMRI study of central sensitisation in patients with migraine

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Introduction: Recent studies indicated that central sensitisation might contribute to the obstinacy and transformation of migraine. Cutaneous allodynia (CA), an easily identifiable marker of central sensitization, develops in more than 60% of migraineurs. However, the mechanism of central sensitisation and its role is still not completely clear. The aim of the present study was to verify the central sensitisation hypothesis in migraineurs and identify relevant cerebral activity using functional magnetic resonance imaging (fMRI).
Methods: A total of 40 migraineurs without aura (20 with CA and 20 without CA) were enrolled, as well as 20 gender- and age-matched healthy controls. CA was assessed by trained neurologists using the Allodynia Symptom Checklist. Participants' brain regions were studied with fMRI when given different intensity of pain stimuli at the skin of the left forearm. We applied a crossover parametric design to distinguish associated cerebral activity of increased pain experience.
Results: When the pain intensity reported by participants were matched, increased activity of the thalamic area and isolated brain stem were found in both migraine groups, compared to the controls. However, only the activation volumes in the brain stem of migraineurs with CA were less than those without CA.
Conclusion: The thalamic regions might play a role in the development of migraine, and the decreased activation of brain stem might contribute to the maintenance of central sensitisation in migraine patients with CA. We will further investigate the correlation between the change of cerebral activity and the transformation from episodic migraine to chronic migraine.

SC223

0.025% capsaicin gel for the treatment of painful diabetic neuropathy: a randomized, double blind, cross-over, placebo controlled trial

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Introduction: 0.075% capsaicin cream is effective in patients with painful diabetic neuropathy (PDN), but its use is limited due to skin reaction. Lower concentration (0.025%) may offer similar benefit with fewer side effects.
Objective: To study the safety and efficacy of 0.025% capsaicin gel in PDN.
Materials and methods: A 20-week, double-blind, cross-over study randomized subjects with PDN to receive 0.025% capsaicin gel or placebo gel for 8 weeks, with wash-out period of 4 weeks between the two treatments. Primary outcome was score change in visual analogue scale of pain severity. Secondary outcomes were score change in short-form McGill pain questionnaires (SF-MPQ), Neuropathic Pain Scale (NPS), proportion of patients who had pain score reduction at least 30% and 50%, and adverse event.
Results: Of the 35 subjects enrolled, 33 completed at least 8 weeks of the treatment period. The baseline characteristics in each group were similar. There was no significant improvement in pain with capsaicin gel, compared to placebo with VAS score (28.8 vs. 34.6, p=0.53). No significant difference between the groups was found in SF-MPQ (10.0 vs. 11.6, p=0.64), NPS (29.4 vs. 31.3, p=0.81). 30% and 50% pain relief was achieved in 22.9, and 17.1% of patients, on capsaicin gel and 34.3 and 31.4% of patients, respectively, on placebo (p=0.50 and 0.77). Capsaicin gel was well tolerated with minor skin reaction.
Conclusions: 0.025% capsaicin gel is safe and well tolerated, but does not provide significant pain relief in patients with PDN.

SC224

Increased prevalence of migraine in patients with unruptured saccular intracranial aneurysms (SIA)

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Background: Rupture of SIA causes thunderclap headache but it remains unclear whether headache in general and migraine in particular is more prevalent in patients with unruptured SIA. In this case-control study we therefore estimate the prevalence of headaches in patients with SIA during 1 year before rupture.
Methods: Prospectively 199 consecutive patients with SIA (103 women and 96 men, mean age 43.2 years) and 194 healthy blood donors (108 men, 86 women, mean age 38.4 years) received a purpose developed semistructured interview. Diagnoses were made according to the International Headache Society criteria. Aneurysms were diagnosed by conventional cerebral angiography.
Results: Headaches in patients with SIA before their diagnostics or rupture were revealed in 123 patients, therefore their 1-year prevalence was 61.8%. The mean duration of these headaches was 14.8 years, the mean age at the beginning of headaches was 30.2 years. These headaches included: migraine without aura (MO) - 78 (39.2%), migraine with aura (MA) - 2 (1%), tension type headache (TTH) - 39 (19.6%), cluster headache (CH) - 2 (1%), post-traumatic headaches (PH) - 2 (1%). 1-year prevalence of headaches in controls was 32.5% (63 patients out of 194), they included: TTH - 45 (23.2%), MO - 17 (8.8%), PH - 1 (0.5%). Among these headaches in patients with SIA and controls only the prevalence of migraine was significantly (4.5 times) higher in patients with SIA (OR 4.5, 95% CI 2.5-7.8, $p<0.0001$).
Conclusions: This is the first study that convincingly shows a significant association between unruptured SIA and migraine.

SC225

Transcranial magnetic stimulation of visual cortex in migraine patients: a systematic review with meta-analysis

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Introduction: We systematically reviewed the literature to evaluate the prevalence of phosphenes and the phosphene threshold (PT) values obtained during single-pulse Transcranial Magnetic Stimulation (TMS) in adults with migraine.
Methods: Controlled studies measuring PT by single-pulse TMS in adults with migraine with or without aura (MA, MwA) were systematically searched. Prevalence of phosphenes and PT values were assessed calculating mean difference (MD) and odds ratio (OR) with 95% confidence intervals (CI).
Results: Fifteen trials, (369 migraine patients and 269 controls), were included. Patients with MA had statistically significant lower PT compared with controls when a circular coil was used (MD: -22.27; 95% CI -33.44 to -11.10); with a figure-of-eight coil the difference was not significant. There was significant higher phosphene prevalence in MA compared with controls (OR: 3.57; 95% CI 1.16 to 10.94). No significant differences were found either in phosphene reporting between patients with MwA and controls, or in PT values obtained by figure-of-eight coil in subjects with MwA versus controls.
Conclusion: These results support the hypothesis of a primary visual cortex hyper-excitability in MA, providing not enough evidence for MwA. A significant statistical heterogeneity reflects clinical and methodological differences across studies, and higher temporal variabilities among PT measurements over time, related to unstable excitability levels. Patients should therefore be evaluated in the true interictal period with an adequate headache free interval. Furthermore, skull thickness and ovarian cycle should be assessed as possible confounding variables, and sham stimulation should be performed to reduce the rate of false positives.

Movement disorders 2

SC226

Clinical features of 14 patients with Parkinson's disease due to an autosomal dominant mutation in the vacuolar protein sorting-associated protein 35 (VPS35)

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Introduction: Up to now five genes causing monogenic autosomal recessive or autosomal dominant (AD) forms of PD have been revealed by genetic studies. Recently, a new AD parkinson mutation (D620N) in the VPS35 gene was discovered by two independent groups (Zimprich et al. 2011, Vilariño-Güell et al. 2011).

Methods: Clinical features of 14 members (8 females) from three affected families were evaluated. The oldest ancestor could be traced back to 1802.

Results: Median age of onset of motor symptoms was 49 years, range 40-68 years. Initial presentations included resting tremor, bradykinesia, rigidity or postural instability. Prevailing signs at last visit were most often resting tremor (12 cases), rigidity (11 cases), bradykinesia (10 cases), asymmetry (all patients), freezing of gait (7 cases), postural instability (9 cases, 7 recurrent falls). All our cases responded to dopaminergic therapy (dopamine agonist and/or levodopa). Median MMSE sum-score in 12 patients was 30/30, ranging from 26 to 30. Median score of the Frontal Assessment Battery, available in 10 patients, was 18/18 points, range 11-18. 7 of 13 patients were suffering from psychiatric symptoms: 5 from depression, 2 from psychosis of those one had a severe drug induced impulse control disorder. Other non-motor symptoms in a subcohort: mild sleeping disturbances were reported by 4 of 6 patients, orthostatic intolerance by 3 patients, gastrointestinal symptoms by one patient (rather due to Mb. Crohn). Hyposmia was detected in 2 patients.

Summary: VPS35 cases showed a somewhat earlier onset, but otherwise similar symptoms to classical sporadic PD.

SC227

Asymmetry of olfactory sulcus depth and relationship with olfaction in Parkinson's disease

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Aims: To assess the depth of olfactory sulcus in relation to olfaction in Parkinson's disease patients.

Methods: MRI scans to measure the depth of the right and left olfactory sulcus in millimetres. Olfactory impairment was measured on UPSIT test. Patients were categorised into groups of anosmia (severe olfactory loss, UPSIT ≤17) and hyposmia (UPSIT >17).

Results: 49 patients were examined, mean age 68±9, range 47-89. Mean sulcus measurements were 5.6±1.1, range 2.55 to 8.85mm. There was no significant difference between the anosmic 5.8±1.3mm vs. hyposmic - 5.3±1.1mm patients for mean sulcus measurement, p=0.17. Left sulcus was significantly smaller than the right, 5.2±1.5 vs. 5.9±1.5mm, p=0.001; mean difference on paired sample test 0.69±1.6mm, p=0.004. There was a significant difference in the right sulcus between anosmic - 6.4±1.6 vs. hyposmic group 5.3±1.2mm, p=0.01; there was no difference in the left sulcus depth between the two groups, 5.2±1.6mm vs. 5.2±1.2mm, p=0.91. There was a significant negative Pearson correlation between right sulcus and the UPSIT values, r=-0.285, p=0.047 but no significant correlation was noticed between olfaction and left sulcus depth, r=-0.019, p=0.89 and for mean depth, r=0.179, p=0.21.

Conclusions: There is a significant asymmetry in the depth of the right and left olfactory sulcus in PD patients; anosmic patients had larger right olfactory sulcus than hyposmic patients. The asymmetry of olfactory sulcus measurement would be consistent with the asymmetry of motor clinical features observed in PD patients.

SC228

Episodic memory in prodromal Huntington's disease: cognitive deficits a decade before diagnosis?

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Introduction: Neurological symptoms may not be detected in prodromal Huntington's disease (HD) and therefore it is often called preclinical or presymptomatic phase. Patients often report concentration, attention, and memory problems before motor symptoms. Our aim was to investigate a broad spectrum of memory functioning in relation to estimated time to clinical disease onset in HD.

Methods: Participants were recruited through a predictive testing program for HD at Karolinska University Hospital, Stockholm. Predicted Years To Onset (PYTO) of HD were calculated using CAG repeats in the expanded allele and current age. Based on genetic information and median split of PYTO three groups were formed: carriers with less than 12 years to disease onset (PYTO<12), carriers with 12 or more years to disease onset (PYTO≥12), and non-carriers. Neuropsychological tests were designed to examine verbal episodic memory using Fuld Object Memory Evaluation and visuospatial ability using Rey-Osterrieth Complex Figure Test, Corsi Block-tapping Test, and Spatial Test.

Results: The PYTO<12 group scored significantly lower than the non-carriers on measures of verbal recall, long-term storage, and retrieval; located fewer objects correctly on the Spatial Test; and scored lower on Corsi Block-tapping Test. These results suggest that episodic, verbal, visuospatial, and working memory are impaired in the prodromal phase of HD before appearance of motor symptoms and/or diagnosis.

Conclusions: The results suggest early dysfunctions in the caudate nucleus and the putamen and in cortico-striatal circuits between the striatum, prefrontal cortex, and parietal lobe approximately 12 years before motor onset of the disease.

SC229

Minimally toxic dose of lipopolysaccharide and α-synuclein elicited synergistic dopaminergic neurodegeneration: role and mechanisms of microglial NOX2

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Introduction: Neuroinflammation characterized by microglial activation is a potential driving force of progressive dopaminergic neurodegeneration in Parkinson's disease (PD).

Objective: To explore the role and mechanisms of microglial superoxide-generating enzyme, beta-nicotinamide adenine dinucleotide phosphate oxidase 2 (NOX2) in minimally toxic dose of lipopolysacchride (LPS) and aggregated α-synuclein (Syn) elicited synergistic dopaminergic neurodegeneration.

Methods: Multiple primary cultures from rodent and NOX2-/- mice were used; Immunostaining was performed for visualizing cell morphology; Superoxide was measured by superoxide dismutase-inhibitable reduction of monosodium salt-1; Real-time PCR and Western blotting were adopted to detect gene and protein expressions; translocation and combination of NOX2 subunits were analyzed by confocal microscopy.

Results: LPS and Syn caused selective, progressive synergistic dopaminergic neurotoxicity in midbrain neuron-glia cultures at the same time or in tandem; it was microglia that mediated synergistic dopaminergic neurotoxicity by LPS and Syn; LPS and Syn synergistically activated microglia indicated by morphological alteration and production of neurotoxic factors, including superoxide and iROS, etc; LPS and Syn increased gene expressions and protein phosphorylations of extracellular signal-regulated kinase, P38, and c-Jun N-terminal kinase and upregulated expressions of protein kinase C and nuclear factor-κB, led to the translocation of P47 (NOX2 cytoplasm subunit) to cell membrane and combination with gp91 (NOX2 membrane subunit), and produced superoxide and subsequent dopaminergic neurodegeneration.

Conclusions: Microglial NOX2 is the target of synergistic dopaminergic neurotoxicity by LPS and Syn, inhibition of microglial NOX2 activation might be a novel strategy for PD therapy.

SC230

Impact of treatment on quality of life in early and drug-naïve Parkinson's disease: the Norwegian ParkWest study

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Introduction: There is limited data on the quality of life (QoL) in early Parkinson's disease (PD). The timing of treatment initiation in PD remains controversial.
Methods: To evaluate QoL and treatment in early PD, 189 drug-naïve patients and 164 controls were included in an open, longitudinal cohort study (The Norwegian ParkWest study). At the time of diagnosis, disease severity and QoL were assessed using validated scores (UPDRS & SF-36). Symptomatic treatment was initiated, and patients were re-assessed after 12 months. Patients were grouped according to treatment at the 12-month follow-up: No dopaminergic treatment or dopaminergic treatment.
Results: At the time of diagnosis, patients with PD have worse QoL-measures than age-/sex-matched controls. Dopaminergic treated patients had worse self-assessed physical health compared to not treated patients. After one year, not treated patients mostly remained stable in terms of motor symptoms and QoL, thus their QoL remained poorer than their healthy controls. Treated patients improved significantly in terms of motor symptoms and mental health. Physical function worsened in the control group but was improved in the treated patients.
Conclusion: For patients with newly diagnosed PD and little impairment, the "wait-and-watch" strategy seems sufficient considering the development of motor symptoms and QoL. However there might be room for improvement in QoL by treatment. As the expected improvement in motor symptoms and physical function in dopaminergic treated patients was also accompanied by an improvement in mental health, our findings may strengthen the policy to treat patients with PD at its earliest stages.

SC231

Abstract cancelled

History of neurology; Neurology and arts

SC232

Neuroscientist victims of the Holocaust

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Introduction: The rise of the Third Reich in 1933 coincides with the decline of the neurosciences and medicine in Germany and Austria. Following the 'Law for the Restoration of the Professional Civil Service', 135 out of 331 faculty members of the Berlin Medical Faculty were dismissed due to racial reasons. At Vienna Medical School 153 of 197 lecturers were forced to leave. Yet many of the discharged scientists opted against emigration because of denial of what the Nazis represented, a sense of assimilation in Germany or Austria, family obligations, or simply the lack of opportunity abroad. The vast majority of those who had not left before 1941 were deported, and most of them did not survive. Also in the occupied Eastern European countries large numbers of neuroscientists were persecuted and perished in the Jewish ghettoes and in extermination camps.

Purpose: This work presents a survey of prominent Holocaust neuroscientist victims, including Ludwig Pick and Arthur Simons (Berlin), Raphael Weichbrodt (Frankfurt), Alexander Spitzer and Victor Frankl (Vienna), Lucia Frey (Lviv) and Wladislaw Sterling (Warsaw). In addition, biographical data from numerous less well-known German, Austrian, and Polish neuroscientists is listed in order to prevent their names from fading into oblivion.

SC233

The neurosciences in the Byzantine era

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Introduction: Neurosciences possessed an important place in medical thought and education of the Byzantine era. Byzantine neurology inherited the classical Greek and Hellenistic medical principles and doctrines, which were harmoniously amalgamated with Christian orthodox spirituality. The medical practice in Byzantium (Constantinople), based on erudition, high medical ethics and charity, has been a work of compassion and mercy. Among the physicians who were distinguished for their special erudition in Neurology we mention Oribasius of Pergamos, Aetius of Amida, Alexander of Tralles, Paulus of Aegina, Theophilos Prorospatharios, Theophanes "Nonnos", Ioannis Zachariou, Nickolaos Myrepsos. The contribution of all of them on the treatment of the neurological and mental diseases exercised an enormous influence on Western Medicine and Pharmacology. The blossom of the Neurosciences in Byzantine era, coincided with the establishment of numerous Hospitals in Constantinople and other major cities. The hospitals in Constantinople gained a genuine scientific profile, with their well organized departments, units for neurological and mental diseases, intensive care units and outpatient clinics. The hospitals disposed their own Pharmacy and Library. Of the most well known Hospitals in Constantinople was Xenon of Pantokrator, a university Hospital founded by the Emperor John B'Comnenos, in 1136. The Typikon of the Hospital offers a unique opportunity to realize how medical care was organized in Byzantium. The hospitals and the neurological and mental units in Constantinople irradiated all over the world the principles of devotion and unselfishness of the doctors, who ministered in the spirit of charity, compassion, mercy and self sacrifice.

SC234

Abstract cancelled

SC235

Tomas Tranströmer's stroke of genius: language but no words

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Introduction: In 1990 the widely acclaimed Swedish poet Tomas Tranströmer lost his speech and the use of his right hand as a result of a stroke. In spite of a severe expressive dysphasia with dysgraphia he has managed to produce some of the best poetry written in the 21st century.

Development: As if anticipating his own fate, in 1974 he referred the story of a composer: "Then, cerebral haemorrhage: paralysis on the right side with aphasia,/ can grasp only short phrases, says the wrong words." An amateur pianist himself, Tranströmer carried on playing left handed piano pieces after the stroke. Interestingly, in 1928 Maurice Ravel composed *The Concerto For The Left Hand in B-Major* for a pianist who had lost his right arm in the Great War, hence enabling him to resume his occupation. Paradoxically, the French composer saw the end of his career arrive in 1933 after losing his speech through a brain insult that left him unable to express his musical ideas in either writing or performance. Psychologist by trade, Tranströmer continued creating poetry in accordance with a 1979 no less prophetic motto "language but no words": a motto somewhat reminiscent of that of the physician-poet and stroke sufferer William Carlos Williams´ "no ideas but in things". Following the stroke, Tranströmer's poetry became even more abbreviated.

Conclusions: As the first anniversary of the Nobel Prize in literature approaches, we celebrate Tranströmer's illuminating poetry. A non-prolific writer prior to having the stroke, a nowadays speechless Tranströmer keeps producing a poetic language of the highest calibre.

Child neurology/developmental neurology; Neurogenetics

SC236

Novel GALC gene mutations in Krabbe's disease

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Introduction: Krabbe's disease or globoid-cell leukodystrophy is an autosomal recessive disorder due to deficiency of the lysosomal enzyme galactocerebrosidase (GALC). 85-90% of the patients have the infantile form presenting with extreme irritability, spasticity and developmental delay before six months of age and death usually before two years of age. 10-15% of the patients have a late-onset form of the disease with onset between six months and the fifth decade and with slower disease progression. Incidence is about 1/100,000. About 80 different mutations have been described as a cause of Krabbe's disease. Some mutations are more common in patients with the classic infantile form of Krabbe's disease of European descent while other mutations are more common in patients of Japanese ancestry. The common 30kb deletion in GALC gene accounts for about 18% of mutant alleleles. Missense, frameshift, nonsense and splice-site mutations have been described as well.
Method: A girl with muscular jerks from age five weeks had the following months irritability, delayed weight gain, possible seizures, some dysrhytmia on EEG and was treated with antiepileptics. GALC enzyme analysis and Array Comparative Genomic Hybridization (ACGH) were performed.
Results: GALC protein analysis showed reduced enzyme activity. Molecular karyotyping with ACGH revealed two mutations, a deletion spanning the complete GALC gene and a partial deletion of the remaining GALC allele i.e. a compound heterozygote.
Conclusion: To our knowledge these mutations have previously not been described. Large scale mutations such as a complete deletion of a gene may be overlooked in ordinary sequencing.

SC237

Models of creatine deficiency syndromes by RNAi in developing brain cells

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Creatine deficiency syndromes, due to deficiencies in AGAT and GAMT, the two enzymes necessary for creatine synthesis, or in the creatine transporter SLC6A8, lead to a complete absence, or a strong decrease, of creatine within the brain, as measured by MRS. CNS is the main organ affected in patients, who show severe neurodevelopmental delay and present neurological symptoms in early infancy (mental retardation, disturbance of active and comprehensible speech, autism, automutilating behaviour, hypotonia or intractable epilepsy). Creatine plays an essential role in CNS to maintain sufficient ATP levels for brain development and functions, and was also recently suggested as neuromodulator or even true neurotransmitter. Recently, we have shown that the blood brain barrier has a limited permeability for creatine, and that the brain must synthesize an important proportion of its own creatine. To better understand creatine deficiencies in developing brain cells, we developed experimental models by gene knock-down through RNAi of AGAT, GAMT and SLC6A8 in 3D organotypic rat brain cell cultures in aggregates, which were transduced by adeno-associated virus (AAV2) expressing specific shRNAs for AGAT, GAMT and SLC6A8. We show that AAV2-transduced RNAi was able to knock down AGAT, GAMT and SLC6A8, strongly affecting brain cell development, as shown by the use of brain cell type (NF-M; GFAP; MBP) and apoptotic (caspase 3) specific markers. AAV2 appear as powerful tools for knocking down AGAT, GAMT and SLC6A8 expression by RNAi in developing brain cells, allowing the analysis of specific alterations of CNS development in creatine deficiency syndromes.

SC238

Patients with West syndrome - what happened after five years?

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Introduction: West syndrome (WS) is an age-dependent epileptic encephalopathy characterized by a clinicoelectrical triad: infantile spasms (IS), hypsarrhythmia and psychomotor delay. The continuing spasms and hypsarrhythmia have a deleterious effect on brain maturation and further cognition and development.
Objective: To determine the factors influencing the long-term prognosis of WS.
Methods: The study comprised of 40 patients (29 boys and 11 girls) with the diagnosis of WS treated at the University Children's Hospital in Belgrade from 1987 to 2008. The age at onset ranged from 2 to 17 months (mean 7.25±3.01) and the follow-up period was at least 5 years. All children underwent a complete physical and neurodevelopmental examination along with detailed history. Patients were divided into three groups according to their response to therapy which was assessed through their developmental response and seizure control.
Results: The response to therapy was good in 32.5%, partial in 47.5% and bad in 20%. Patients with no significant developmental delay (7.5%) as well as those with a certain degree of neurodevelopmental improvement in the course of treatment (35%) had more favourable outcome. Complete control of seizures was attained in 75% and correlated significantly with the outcome.
Conclusion: Although West syndrome is regarded as one of intractable epilepsies, the prognosis differs widely. Our study has shown that the mild nature of psychomotoric regression and prompt improvement of clinical status under treatment are factors associated with a good long-term prognosis of WS. Severe psychomotor impairment and repeated seizures were prognostic of poor outcome.

SC239

Cerebellum – more than motor control? Cognition in spinocerebellar ataxia type 14

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Spinocerebellar ataxias SCA 1-36 are dominantly inherited degenerative ataxias. The symptoms are due to progressive cerebellar impairment with ataxia, and varying degrees of associated symptoms such as neuropathy, parkinsonism and cognitive failure. Extracerebellar involvement in some SCAs gives a phenotype with marked cognitive failure, but mild cognitive impairment in pure cerebellar SCAs is reported. SCA14 is recently identified in Norway, and the phenotype appears to have little extracerebellar involvement. There is increasing awareness of cognitive impairment in cerebellar disorders, possibly due to degeneration of cortico-cerebellar connections. Our hypothesis is that there is a frontal cognitive impairment associated with SCA14.
Material: 10 patients with confirmed SCA14 and 10 healthy matched intrafamiliar controls were tested with standardized ataxia-score and neuropsychological tests, focusing on psychomotoric speed, attention, learning, memory, intelligence and executive functions. Tests were chosen to minimize manual response due to possible ataxia-related confounder.
Results: Compared to international age-standardized norm data, the patients showed significant impairment in verbal abilities, psychomotoric speed, working memory and visual learning. The controls also tended to show impairment to norm data. Compared to controls, patients showed significantly better verbal learning. Regarding cognitive flexibility and visuospatial function, there was a trend towards lower performance among the patient group. Longer disease duration correlated with better cognitive flexibility. No correlation between severity of ataxia and cognitive performance was found.
Conclusion: These SCA14 patients show significantly impaired function in several neuropsychological domains compared to standardized norm data, and a trend towards lower performance in corresponding domains compared to intrafamiliar controls.

SC240

Polymerase gamma (POLG) associated encephalopathy is characterised by neuronal mtDNA depletion and respiratory complex-I deficiency

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Background: Polymerase gamma (POLG) mutations cause encephalopathy syndromes with ataxia, epilepsy and stroke-like episodes. Although well described clinically, the molecular pathophysiology of POLG encephalopathy remains largely unknown and few studies have been performed on human brain, which is the organ primarily affected by the disease.
Materials and methods: We studied an extensive post-mortem material including samples from all major areas of the central nervous system (CNS) from 9 patients with POLG-encephalopathy and 8 controls. Our studies include structural histology, histochemical and immuno-histochemical studies of the respiratory chain and mtDNA analyses in tissue homogenates and microdissected neurons.
Results: Both mtDNA deletions and depletion occur in neurons of patients with POLG encephalopathy, but showing the latter requires single cell analysis. Depletion is more pronounced (50-70%), appears to be an early phenomenon and correlates with disease severity. Multiple deletions are less prominent (0-40%) and appear later, gradually increasing with disease duration. Respiratory chain studies show predominantly neuronal complex-I deficiency with a predilection for certain areas including the cerebellar cortex, dentate and olivary nuclei. Complex-IV deficiency is milder and increases with disease duration. No abnormalities are seen in the remaining complexes.
Conclusions: Our findings suggest that neuronal mtDNA depletion is an early event in POLG encephalopathy and may be the main factor driving mitochondrial dysfunction, primarily via complex-I deficiency. MtDNA deletions occur later and gradually accumulate during the course of the disease along with complex-IV deficiency, suggesting that these may play a secondary or bystander role in disease development in the nervous system.

SC241

Comparative genome hybridization with high-density oligonucleotide microarrays in sib pairs with sporadic Parkinson's disease

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Introduction: Comparative genome hybridization (CGH) with high-density oligonucleotide microarrays is a novel valuable tool for the detection of clinically-relevant copy number variations (CNVs).
Objective: To detect CNVs critical for PD risk by comparing genomes of sib pairs consisting of a Parkinson's disease (PD) patient and his/her healthy brother or sister.
Patients and methods: CGH was performed with human SurePrint CGH 1M oligonucleotide microarrays (Agilent) in 16 PD sib pairs of Polish ethnicity.
Results: We detected 26 distinct CNVs across genome that occurred significantly more frequently among PD patients compared to their healthy sibs. The PD-associated CNVs contained several genes implicated in intrinsic and environmental toxin inactivation, neurotransmitter processing and release as well as neurodegeneration.
Conclusion: The CGH analysis in PD sib pairs identified novel genomic regions potentially involved in PD development.