Cephalalgia
An International Journal of Headache
International Headache Society

Cephalalgia
2015, Vol. 35(6S) 1–296

DOI: 10.1177/0333102415581304
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International Headache Society abstracts

ScS1-1

Special Session 1 – Headache Trainees Excellence Tournament

Propagation of cortical spreading depression reduced by 5HT1 receptors alternation

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The migraine attack has been observed to be associated with cortical spreading depression (CSD) associated with low level of serotonin (5-HT). However, the mechanism underlying this phenomenon is still unclear. The development of serotonin receptor agonists in alleviation of migraine pain in clinical trials, further implicates the role of serotonin as a key molecule in migraine. In this regard, present study evaluated the role of 5-HT1 receptor on electrophysiological parameter of the cortical spreading depression (CSD). Wistar rats ($n = 28$) were injected interventricular with fluoxetine (5, 10, 20 mg/kg) and/or saline. CSD was recorded immediately after KCl (3 mM; 10–15 μl) injection. In addition, all groups were CSD-recorded for 60–70 min. The interventricular fluoxetine injection effect was reverted after flushing the treated region with saline. Fluoxetine applied during the CSD-induction period. CSD-velocities reduced significantly in 10 and 20 mg/kg ($P < 0.05$). Also amplitude and duration of CSD waves were significantly decreased in 5, 10, and 20 mg/kg of fluoxetine ($P < 0.05$). The present effect of fluoxetine, supports the hypothesis of a serotoninergic influence on CSD, as previously suggested in experiments using other serotoninergic drugs.

Keywords: Serotonin, Migraine, Electrophysiology, Spreading Depolarization

IS02

Special Session 1 – Headache Trainees Excellence Tournament

Altered white matter tract integrity in patients with prolonged post-concussion symptoms

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Introduction: Routine structural neuroimaging is typically normal following concussion, even in patients who have a multitude of post-concussion symptoms.

Diffusion Tensor Imaging (DTI), which allows for the interrogation of white matter tract integrity, has been useful in determining brain alterations in acutely concussed patients, yet the existence of white matter alterations in patients with prolonged post-concussion symptoms (>1 month) remains controversial.

Methods: Using global probabilistic DTI tractography, we examined the integrity of several major fiber tracts in 12 concussed patients (age = 36.0; SD = 15.9) who continued to be symptomatic at least 1 month post-concussion but had normal routine T1 and T2 imaging and in 12 healthy, age-matched control subjects (age = 38.9 SD = 13.0).

Results: Concussed patients showed higher axial diffusivity (AD) but unchanged fractional anisotropy (FA) in the right (AD: $p = .043$; FA: $p = .545$) and left (AD: $p = .022$; FA; $p = .066$) superior longitudinal fasciculi and higher AD ($p = .035$) and lower FA ($p = .044$) in the forceps major relative to controls. No significant group differences in tract FA and AD were found for the left (AD: $p = .706$; FA: $p = .485$) and right (AD: $p = .673$; FA: $p = .904$) uncinate fasciculus. Exploratory post-hoc analyses indicated that patients with multiple concussions ($n = 6$) had higher FA in the left superior longitudinal fasciculus ($p = .02$) relative to

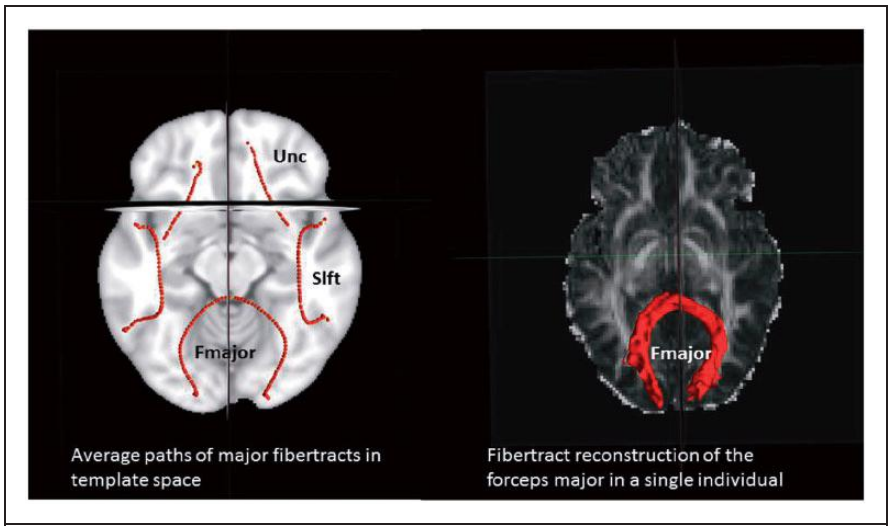

Figure. Fmajor = forceps major; Unc = uncinate fasciculusl; Slft = superior longitudinal fasciculus.

patients with one concussion (n = 6). No other tract metric differences were identified.

Conclusion: In patients with persistent symptoms, white matter tract integrity is altered beyond 1 month following concussion. Tract damage might be more extensive in patients with multiple concussions.

IS03

Special Session I – Headache Trainees Excellence Tournament

Trigeminovascular cgrp release in familial hemiplegic migraine type 1 knockin mice

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Background: Neuronal hyperexcitability has been shown in transgenic knockin mice carrying the familial hemiplegic migraine type 1 (FHM1) mutations in the *Cacna1a* gene. However, the effects of FHM1 mutations on the trigeminovascular system and the release of neuropeptides are largely unknown.

Aim: To investigate the release of calcitonin gene-related peptide (CGRP) in the absence and presence of the antimigraine drug, sumatriptan, in different components of the trigeminovascular system in FHM1 mice with the R192Q missense mutation.

Method: Dura mater, trigeminal ganglion (TG) and trigeminal nucleus caudalis (TNC) were isolated from adult R192Q mice. Tissues were triggered with 60 mM KCl in the absence or presence of sumatriptan (30 μM). Supernatant was collected for CGRP measurements. Data are expressed as relative stimulated CGRP release (mean ± s.e.m). This study is approved by the ethics committee of the Erasmus Medical Center in Rotterdam

Results: We found no difference in KCl-induced CGRP release in different components of the trigeminovascular system between R192Q (dura mater: 5.8 ± 2.0, TG: 5.0 ± 1.9, TNC:4.9 ± 1.1) and wildtype (dura mater: 16.1 ± 5.7, TG:5.9 ± 1.7, TNC:6.4 ± 1.2) mice. Sumatriptan only inhibited the CGRP release in the TNC (control: 4.7 ± 1.1, sumatriptan: 2.6 ± 1.0) and dura mater (control: 5.7 ± 3.3, sumatriptan: 0.8 ± 0.1) of wildtype but not in R192Q (TNC; control: 5.3 ± 1.3, sumatriptan: 3.4 ± 1.0 and dura mater; control: 4.8 ± 2.2, sumatriptan: 5.6 ± 3.2) mice.

Conclusion: KCl-induced CGRP release seems unaffected by the R192Q mutation, in contrast with earlier findings in TG of younger R192Q mice (Fioretti et al. (2011), J. Physiol, 589.23). Interestingly, sumatriptan reduced trigeminovascular activation in the wildtype but not in the R192Q mice, suggesting a disinhibition of the trigeminovascular system.

IS04

Special Session I – Headache Trainees Excellence Tournament

Feasibility of using structural brain data for diagnosing migraine

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Background: Migraine is diagnosed using operational criteria according to ICHD II/III-beta. Changes in brain structure or function, or other biomarkers are not currently considered in the diagnostic process.

Aim: Using multicenter high-resolution structural MRI data, we tested the ability of a machine learning technique to distinguish migraineurs from healthy subjects on the basis of cortical thickness and subcortical morphology.

Methods: T1-weighted MPRAGE data of 131 migraineurs (40 with aura; 31 ± 9yo; 109 women; monthly attack frequency: 3.2 ± 2.5; disease duration: 14 ± 8.4y) and 115 matched healthy subjects (29 ± 7yo; 81 women) acquired at four different centers at 3 Tesla were pooled. Cortical thickness and subcortical morphology were assessed using FreeSurfer and MAGeT. A linear support vector machine (SVM) algorithm was used to determine the diagnostic accuracy in separating migraineurs from healthy subjects based on 90 unselected variables (cortical thickness in distinct gyri and subcortical volumes; 70% of data used for training of classifier, 30% for classification). Another SVM was trained to distinguish migraineurs with versus without aura. Age, gender and center were included in both analyses.

Results: The SVM classifier yielded an accuracy of 74.4% (sensitivity 71.4%, specificity 77.8%) for distinguishing migraineurs from controls. An accuracy of 85% (sensitivity 83.3%, specificity 85.7%) was reached when separating patients with from those without aura.

Conclusion: The data support the view that migraine is a brain disorder with distinctive cortical/ subcortical anatomical features. Although the diagnostic accuracy currently remains too low for clinical practice, it is a good starting point for a future supplementary diagnostic tool.

IS05

Special Session I – Headache Trainees Excellence Tournament

Pain related cortical and subcortical grey matter changes in cluster headache

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Background: Subcortical structures, like the basal ganglia, thought to have a crucial role in pain processing, which was underlined by neuroimaging studies detected activation in these areas in acute and chronic pain.

Aim: In the current study we investigated the cortical and subcortical grey matter volume in cluster headache patients.

Method: High-resolution T1 weighted images were acquired from seventeen CH patients and thirty-one age-matched healthy controls. Voxel based morphometry with threshold-free cluster enhancement statistic and surface based subcortical segmentation analysis were used to measure the cortical thickness and the volume of the subcortical nuclei. Data was mirrored to the pain-affected right side. Correlation of the size of the subcortical structures and cumulative number of headache days was examined in patients.

Results: The left posterior and central opercular grey matter density decreased in cluster headache patients compared to controls ($p < 0.02$), contralateral to the pain affected side. The volume of the right caudate nucleus and pallidum decreased in patients. The cumulative number of the headache days showed positive correlation to the right hippocampus volume ($p < 0.046$, $R = 0.490$).

Conclusion: Structural analysis of basal ganglia and the cortical grey matter in cluster headache provides important features of the disease. While the grey volume changes seem to be a key to the pathogenesis of cluster headache, further structural and functional investigations are needed to understand deeply the pathomechanism of this headache type.

IS06

Special Session I – Headache Trainees Excellence Tournament

Non-paralytic botulinum chimeras increase the activation threshold of the trigeminovascular system in migraine models

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Background: Botulinum toxin injections are an established preventive treatment for migraine. However, it remains inconclusive whether the unwanted muscle paralysis has an involvement in the mechanism of treatment. Clostridial chimeras that lack this paralytic effect have been recently developed. These novel recombinant toxins can selectively target sensory over motor neuronal fibres.

Aim: To investigate the efficacy of two Clostridial chimeras with a reduced paralytic activity, Bitox and Tetox, in the migraine animal model of trigeminovascular activation.

Methods: Bitox, or Tetox (200 ng) were injected over one peri-orbital area (100 nl), while saline was injected contralaterally. Forty-eight to 72 hours later, the animals were tested for blink reflex, as an indication of muscle paralysis. Following, mechanical (von Frey) and trigeminovascular activation thresholds were assessed blindly bilaterally on second order neurons in the trigeminocervical complex in anaesthetised animals.

Results: None of the animals demonstrated muscle paralysis during the blink reflex test. Overall, both chimeras significantly increased the mechanical thresholds compared to the control side ($P < 0.005$). Activation thresholds of second order neurons, assessed as the minimum voltage required to induce evoked action potentials, were significantly increased following treatment with chimeras compared to saline ($P < 0.005$). Bitox was marginally superior to Tetox, however, this did not reach significance. No differences in the basal levels of spontaneous neuronal activity were observed between the three treatments ($P = 0.47$).

Conclusion: Non-paralytic botulinum-like chimeras can be important modulators of trigeminovascular nociceptive processing, potentially offering a significant advancement in the preventive therapeutic options for patients.

OR01

Proof of concept clinical trial of ALD403, an anti-calcitonin gene-related peptide (CGRP) antibody in the prevention of migraine – 6 month data

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Background: CGRP is involved in the pathophysiology of migraine. We evaluated the efficacy and safety of ALD403, a humanized anti-CGRP antibody, for migraine prevention.

Methods: Patients with 5 to 14 migraine days per month were randomized to receive a single intravenous dose of ALD403 1000 mg or placebo. The primary endpoint was the mean change in migraine headache days from baseline to weeks 5–8. Patients were followed for 24 weeks for additional safety and efficacy analyses.

Results: Of 174 patients randomized, 163 patients received either ALD403 (81) or placebo (82). There were no significant differences in baseline demographics

or characteristics between the two treatment groups. The proportion of patients with a 50%, 75%, and 100% reduction in migraine days for weeks 1–12 for ALD403 and placebo was 61% vs 33% ($p < 0.001$); 33% vs 9% ($p < 0.001$); and 16% vs 0% ($p < 0.001$), respectively. The proportion of patients with a 50%, 75%, and 100% reduction in migraine days for the entire 24 weeks for ALD403 and placebo was 53% vs 28% ($p < 0.001$); 26% vs 7% ($p < 0.002$); and 11% vs 0% ($p < 0.002$), respectively. Safety data over 24 weeks were comparable between both treatment groups.

Conclusions: A single intravenous dose of ALD403 1000 mg demonstrated prolonged efficacy (over 6 months) for the preventive treatment of migraine. ALD403 was safe and well tolerated. These results support the conduct of larger randomized, placebo-controlled studies and may represent a new era in disease-specific and mechanism-based preventive therapy for migraine.

OR02

Results of a randomized, double-blind, placebo-controlled, phase 2 study to evaluate the efficacy and safety of AMG 334 for the prevention of episodic migraine

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Background: Migraine is a disabling neurological condition. Calcitonin gene-related peptide (CGRP) has been implicated in migraine pathogenesis. AMG 334 is a fully human monoclonal antibody that inhibits the CGRP receptor.

Aim: To evaluate the effects of AMG 334 in preventing episodic migraine.

Methods: Patients were randomized to subcutaneous, monthly placebo or AMG 334 (7 mg, 21 mg or 70 mg) in a 3:2:2:2 ratio, respectively. The primary endpoint was the change from baseline in monthly migraine days at week 12. Secondary endpoints included 50% responder rate, monthly migraine attacks, and safety/tolerability. Key exploratory endpoints included monthly headache days and monthly acute migraine-specific medication use days (ie, triptans, ergotamines). This study was approved by the institutional review board/ethics committee for each site. All subjects provided written informed consent.

Results: 483 subjects were randomized. A statistically significant reduction in monthly mean migraine days was observed with AMG 334 70 mg (−3.40) vs placebo (−2.28); $P = 0.021$; lower doses (7 mg and 21 mg) were not statistically significant (Figure). The 50% responder rate was 46.5% for 70 mg vs 29.9% for placebo ($P = 0.011$). Statistically significant reductions in monthly headache days (70 mg: −3.54 vs placebo: −2.39; $P = 0.022$) and monthly migraine-specific medication use days (70 mg: −1.64 vs placebo: −0.69; $P = 0.004$) were also observed. The change in monthly migraine attacks was not statistically significant. No major safety findings were reported. The tolerability profile was similar between AMG 334 and placebo.

Conclusion: AMG 334 70 mg demonstrated efficacy in prevention of episodic migraine, with a safety/tolerability profile similar to placebo in this phase 2 study.

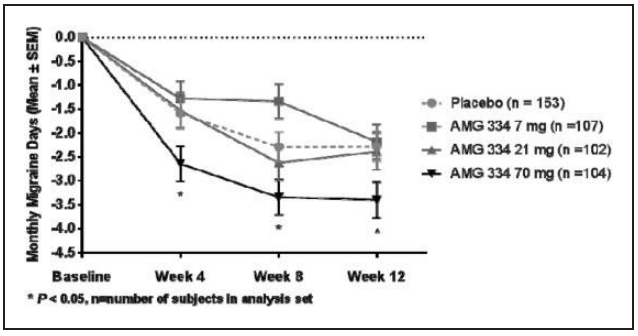

Figure. Change from baseline in mean monthly migraine days.

OR03

Function and expression of two calcitonin gene-related peptide receptors within the sensory trigeminal system

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The trigeminovascular system plays a central role in the pathogenesis of migraine, a condition in need of new treatments. To identify potentially novel neuronal G protein-coupled receptor (GPCR) targets for migraine we determined global GPCR expression in isolated rat trigeminal ganglia neurons using Taqman GPCR arrays. These arrays revealed the expression of numerous GPCRs proposed to be important in pain and inflammation, including the calcitonin gene-related peptide (CGRP) receptor (calcitonin receptor-like receptor [CLR]/receptor activity-modifying protein 1 [RAMP1]). Notably, the array revealed, and antibodies confirmed, the expression of the molecular components of a second CGRP-responsive receptor (calcitonin receptor [CTR]/RAMP1; the AMY_1 receptor). Assessment of responses to several agonists and antagonists in primary trigeminal ganglia neurons revealed a dual population of functional CGRP-responsive receptors. To evaluate the importance of the canonical CGRP receptor in pain we challenged CLR- and RAMP1- deficient mice using tests of mechanical or thermal nociception. Although RAMP1-deficient mice had a large change in response, CLR deficiency did not affect mechanical pain responses, suggesting that CLR may not mediate all pain responses to CGRP. CTR and RAMP1 were detected by immunofluorescence staining in post-mortem human trigeminal ganglia and the major central components of the spinal trigeminal complex in the brainstem (spinal trigeminal nucleus/tract). Co-expression of both proteins was found in discrete areas. These findings, which demonstrate a non-canonical CGRP receptor in neural tissue, prompt a re-evaluation of current therapeutic strategies and new approaches for migraine and pain management..

OR04

Occipital glutamate in interictal migraine patients measured with 7T MR spectroscopy (MRS)

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Background: Glutamate has been implicated in migraine pathophysiology but it is unknown whether and to what extent intra- or extracellular cerebral concentrations of glutamate are different in migraine patients.

Aim: To determine the occipital glutamate concentration and its time-correlated compartment-specific characteristics in interictal migraine patients.

Method: Case-control study with interictal migraine patients with and without aura, and age and gender matched healthy controls. We used 7T MRS with a single volume of interest (VOI: 2x2x3cm) located in the occipital lobe. For ^{1}H-MRS we used a semi-LASER sequence (TR/TE = 5000/30 ms) with water referencing for absolute quantification. For diffusion weighted spectroscopy we used an adapted PRESS sequence (TR/TE = 2000/120 ms) with three directions and two different gradient strengths. Between groups differences were evaluated using ANCOVA with the gray matter fraction in the VOI as covariate and post-hoc comparisons with Bonferroni correction.

Results: Migraine patients with ($n = 23$) and without aura ($n = 27$) and healthy controls ($n = 24$) were included. The glutamate concentrations differed across groups ($p = 0.047$). In a post-hoc analysis the glutamate concentration was increased in migraine without aura (mean $\pm$ SD: 7.02 ± 0.50 mM) compared with controls (mean $\pm$ SD: 6.40 ± 0.78 mM, $p = 0.042$). The apparent diffusion coefficient of glutamate did not differ among groups ($p = 0.129$). There were no other differences in concentrations or diffusion of other metabolites.

Conclusion: Glutamate is increased in the occipital cortex of patients with migraine without aura without observable differences in glutamate diffusion characteristics.

OR05

A pedigree of paroxysmal extreme pain disorder with short-lasting, unilateral headaches and ipsilateral facial flushing caused by a novel SCN9A mutation

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Introduction: We experienced a family with childhood-onset, short-lasting, unilateral headaches characterizedby defecation-induced headaches and genital pain, as well as ipsilateral facial flushing after severe attacks.

Patients and methods: In this family, focal hyperperfusion of the right trigeminal root entry zone was seen during a right-sided attack in one child; in another, left-sided temporal headache attacks were provoked by bilateral electrical stimulation of the upper extremities. Whole exome sequencing of DNA from this family was performed to determine the genetic causality.

Results: We identified a novel *SCN9A* mutation (NM_002977: c.5218G > C, p.Val1740Leu) in all affected family members but not in the unaffected members. *SCN9A* encodes the voltage-gated sodium-channel type IX alpha subunit, known as $Na_v1.7$.

Conclusions: Gain-of-function mutations in $Na_v1.7$ are well known to cause paroxysmal extreme paindisorder (PEPD), which is a painful Na-channelopathy that is characterized by attacks of excruciating deep burning pain in the rectal, ocular, or jaw areas. This is the first report of PEPD with headaches. The *SCN9A* mutation found in this family suggests a broader phenotype of PEPD than previously thought and supports the idea that Na-channelopathy may bethe major genetic cause of short-lasting, unilateral headaches.

OR06

Clinical characteristics of primary headaches in children younger than 6 years

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Background: Those who deal with children with primaryheadache experience difficulties in using the ICHD criteria, due to their weaksensibility in pediatric age.

Aim: To describe the clinical characteristicsof headache in a cohort of children aged <6 years.

Methods: Onlychildren with primary headache were included. Characteristics of the referredpain, frequency of headache and duration of headache attacks were analyzed. Accompanying symptoms were also investigated, particularly nausea, vomiting,photo- and phonophobia.

Results: 368 patients (mean age: 4.4 ± 1.22 years) were eligible for our study (Males: 48.9 % and Females: 51.1%). The duration of attacks was less then 1 hour in 70.8% of cases. We found thatnausea was present in 22.1% of cases, vomiting in 23.3%, photophobia in 42.6%,and phonophobia in 44.1%. One or more periodic syndromes of childhood werefound in more than 50% of children. When we tried to classify patientsaccording to the ICHD-III beta version criteria, more than 31,61% ofpatients did not fulfill criteria for migraine or tension-type headache, thusthe diagnosis remained undefined. After removing the item concerning theheadache attack duration from the ICHD-III criteria, the undefined diagnosesdropped to 16%.

Conclusion: A strict applicationof the ICHD-III criteria for primary headaches to very young children preventsa definite classification of most patients. Since a precise definition theheadache attack duration is very difficult to be obtained from very youngchildren, this criterion should be removed in order to increase theeffectiveness of the ICHD-III criteria.

OR07

Integrating migraine gwas data with brain expression information for functional interpretation of migraine-associated snps

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Background: Genome-wide association (GWA) studies in migraine have identified single nucleotide polymorphisms (SNPs) in over a dozen genome-wide significant loci (surpassing the p-value threshold of $5x10^{-8}$) that affect risk for migraine. Gene-based analyses of GWAS data (including SNPs with higher p-values) can be used to ultimately identify pathways, brain regions, and even cell types involved in migraine pathophysiology.

Aim: Here we aimed to functionally interpret existing GWAS data in a gene-based statistical approach by making use of publically available brain gene expression information.

Method: We performed gene set enrichment analyses in migraine GWAS data from the International Headache Genetics Consortium, utilizing brain-related gene sets based on published glial cell-specific gene expression information and detailed spatial brain gene expression data from the Allen Brain Atlas. GO-term and pathway analyses were used for functional interpretation of the results.

Results: Migraine GWAS signals showed enrichment of gene sets highly expressed in the cortex containing genes involved in neurotransmission. In addition, a gene set highly expressed in subcortical brain areas such as the thalamus and the brainstem including genes involved in myelination showed enrichment in the GWAS data. The glial cell-specific analysis indicated enrichment of oligodendrocyte-specific genes.

Conclusion: Gene-based analyses of GWAS data, making use of publically available expression data from relevant tissues, point towards involvement of cortical neurons as well as oligodendrocytes from subcortical areas in migraine pathophysiology.

OR08

The functional consequence of the ck1δ t44a mutation on nociceptive activation of the trigeminocervical complex

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Background: The CK1δ T44A mutation is associated with the familial advanced sleep phase syndrome (FASPS) and migraine with aura. Preclinical studies have revealed that animals carrying the mutation have a reduced threshold for the induction of cortical spreading depression (CSD).

Aim: The aim of the study was to study the functional consequence of a missense mutation in the casein kinase Iδ gene (CK1δ T44A) in an *in vivo* transgenic mouse model of nociceptive trigeminovascular activation.

Methods: Transgenic mice carrying the T44A mutation (CK1δ T44A) or an additional wildtype gene (CK1δ WT-TG) were compared to non-transgenic wildtype littermates (WT). Superior sagittal sinus (SSS) was electrically stimulated for two hours. Mice were then euthanized and tissue sections of lamina I–IV between Sp5 and C3 were stained for Fos-protein. Fos-positive cells were counted unilaterally.

Results: In WT and CK1δ WT−TG mice electrical stimulation of the SSS induced an increase in Fos expression compared to sham animals. Electrical stimulation did not increase Fos-expression in CK1δ T44A mice. CK1δ T44A sham mice showed an elevated Fos-expression compared to WT and CK1δ WT-TG sham mice reflecting a higher degree of neuronal activity in the TCC which did not increase any further following electrical stimulation of the SSS.

Conclusions: While previous results indicate that the CK1δ T44A mutation is associated with an elevated susceptibility for CSD induction, our results show that the mutation reduces the responsiveness of the TCC to dural stimulation. These observations suggest a supra-medullary focus for the pathophysiology of migraine in these patients.

OR09

Prevalence of migraine in persons carrying the 3243A>G mutation in mitochondrial DNA

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Objectives: Over the last three decades mitochondrial dysfunction has been postulated to be a potential mechanism in migraine pathogenesis. We investigated the lifetime prevalence of migraine in persons carrying the 3243A>G mutation in mitochondrial DNA.

Methods: In this cross-sectional study, we included 57 persons with mDNA3243A>G mutation between May 2012 and October 2014. As control group, we used a population-based cohort from our epidemiological studies on migraine in Danes. History of headache and migraine was obtained by telephone interview, based on a validated semi-structured questionnaire, performed by trained physicians.

Results: The prevalence of migraine is significantly higher in persons carrying the 3243A > G mutation than in controls (58% vs. 18%; $p = <0.001$). This applies for both subforms of migraine; migraine without aura (MO) (47% vs. 12%; $p = <0.001$) and migraine with aura (MA) (18% vs. 6%; $p = <0.001$), and in females (58% vs. 24%; $p = <0.001$) and males (58% vs. 12%; $p = <0.001$) for any migraine.

Interpretation: We found a high prevalence of migraine in persons with the mDNA3243A > G mutation. This finding suggests a clinical association between a monogenetically inherited disorder of mitochondrial dysfunction and susceptibility to migraine. Mitochondrial DNA aberrations may contribute to the pathogenesis of migraine.

OR10

Genome-wide meta-analysis of migraine in 59,000 cases and 316,000 controls reveals 29 new loci, increasing the total number of known risk LOCI to 42

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Background: Relatively little is known about the molecular mechanisms that contribute to the susceptibility to common migraine. This makes hypothesis-generating approaches like locus identification via genome-wide association studies (GWAS) a powerful way to try to dissect migraine pathophysiology.

Aim: In this study, we carried out the largest genetic migraine meta-analysis to date, consisting of 59,673 cases and 316,078 controls. The participants were recruited from six headache centers and 27 population cohorts in the International Headache Genetics Consortium (IHGC).

Method: We performed a fixed-effects meta-analysis of GWAS data from 33 cohorts. Our primary analysis investigated all migraine, while secondary analysis investigated signals specific to MA or MO, as well as *in silico* interpretation of the primary findings.

Results: We report 29 new genome-wide significant loci for migraine, including the first locus on the X chromosome, bringing the number of reported loci to 42. Seven of the 42 loci were found to be specific to MO and no loci were found for MA, perhaps suggesting a hypothesis that rare variation may be central in MA. Follow-up analyses suggest several functional mechanisms to be enriched within the associated loci, including cell signaling and ion homeostasis.

Conclusion: In summary, we report 29 new genetic loci affecting migraine risk, increasing the total number of genome-wide significant loci in common migraine to 42. Preliminary results point to a role for several molecular processes in the brain, but also implicate several genes with previous vascular-disease associations, thus supporting both neuropathic and neurovascular mechanisms for migraine pathophysiology.

OR11

Epidemiology of headache in China

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Headache disorders are among the most common disorders of the nervous system, bringing the heavy burden not only to individual but also to the society all over the world. As is known to all, China is the world's most populous country, with a population of over 1.35 billion. A population-based door-to-door survey was held to estimate the prevalence and burden of primary headache disorders for adults in the general population of China from 2008 to 2009. The survey was completed by 5041 nonrelated adults in six regions of China. Overall, 1425 respondents reported headache in the preceding year, giving a 1-year prevalence of 28.5%. The estimated

1-year prevalence of primary headache disorders was 23.8%, of migraine 9.3%, of tension-type headache (TTH) 10.8%. According to the epidemiological survey, the total estimated annual cost of primary headache disorders, including migraine, TTH, and CDH was CNY 672.7 billion, accounting for 2.24% of gross domestic product (GDP).

OR12

An abnormal transduction of the chromatic stimuli from the outer to the inner retinal layers may contribute to the mechanism of photophobia in migraine

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Background – Recent experimental evidences point out a possible involvement of outer and inner retinal layers in hypersensitivity of migraine patients to light stimuli.

Aim: To investigate the short-wavelength-sensitive (S) and the medium/long-wavelength-sensitive (ML) cone photoreceptors of the visual pathways in migraine without aura (MO) patients between attacks and in healthy volunteers (HV) by using yellow-blue (Y-B) or red-blue (R-B) visual flicker stimuli.

Method: Square-wave focal electroretinograms (FERGs) were recorded in 22 MO patients and 20 HV. For each randomly presented flicker stimulation protocol (Y-B or R-B), 600 sweeps (4 Hz repetition rate) were recorded and partitioned in 6 blocks of 100. Fourier analysis allowed extracting from the FERG data the fundamental (1F) and the second harmonic (2F) components (amplitude and phase) that are related respectively to outer and inner retinal activity. Usual headache severity and photophobia during migraine were scored on a 0 to 10 visual analogue scale.

Results: When compared to HV, MO patients had an advanced 1F phase but normal amplitude in all blocks of Y-B FERG. In MO patients, the self-rated intensity of ictal photophobia was positively correlated with attack frequency ($r = 0.571$, $p = 0.01$), headache severity ($r = 0.508$, $p = 0.03$), 1F Y-B phase (all blocks $r = 0.487$, $p = 0.04$), 1F R-B phase ($r = 0.521$, $p = 0.03$), 2F Y-B amplitude (all $r = 0.610$, $p < 0.01$), habituation slope ($r = 0.686$, $p < 0.01$), and 2F R-B phase ($r = 0.526$, $p = 0.03$).

Conclusion: These results suggest that an abnormal signal transduction from the outer to the inner retinal layers could contribute to the mechanisms by which light causes pain or discomfort during the migraine headache.

OR13

Perfusion changes during migraine without aura attacks an arterial spin labeling MRI perfusion study

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Background: Studies of brain perfusion during attacks of migraine without aura are scarce and have inconsistent results.

Objective: To study global brain perfusion during a spontaneously occurring untreated migraine without aura attack using Arterial Spin Labeling (ASL) MRI.

Methods: Prospective study including two ASL-MRI scans (3 Tesla Siemens Verio MRI) of the same individual first during a spontaneous untreated migraine without aura attack and later in a headache free period. Image analysis used FSL and MATLAB; Group analysis was then performed using Permutation methods in order to identify voxels with statistically significant perfusion differences between migraine and migraine-free sessions.

Results: Thirteen women were scanned, with an age average of 35.7 years and average disease duration of 23 years. The evaluated migraine attack had an average intensity of 6.8 (VAS) and an average duration of 16 hours. No global or regional perfusion differences were identified in the attack, when compared to the baseline scan.

Discussion: This is the first study of brain perfusion during attacks of migraine without aura using the ASL-MRI technique. Our results substantiate that the painful phase of migraine without aura attacks does not involve changes in brain perfusion.

OR14

Microvascular passage and calculation of the transfer constant for [51CR]EDTA and water content in rat ganglion and cns following dural application of freund's adjuvant/inflammatory soup

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Background: Migraine is a paroxysmal, disabling primary headache that involves up to 16% of the adult population. In spite of decades of intense research, the origin and the pathophysiology mechanisms are still enigmatic. Although triptans and gepants provide effective relief from acute migraine for many patients, their site of action remains unknown. It has been suggested that during migraine attacks the leakiness of the blood-brain barrier (BBB) is altered.

Aim: In order to address this issue we performed a series of experiment in rat by induction of local inflammation with Complete Freund's adjuvant (CFA) or the Inflammatory Soup (IS) and quantified the passage of a tracer molecule.

Results: We observed that [^{51}Cr]-EDTA did not pass into the CNS in a major way. However, [^{51}Cr]-EDTA readily passed the trigeminal ganglion by >30 times compared to the CNS. Application of CFA or IS (studied at 2, 24 or 48 hours after the application) did not show altered transfer constant to [^{51}Cr]-EDTA. Myograph studies demonstrated that CFA had no obvious direct vasomotor effect while IS potently constricted isolated middle meningeal arteries.

Conclusions: Thus, with these experiments we suggest (i) that dural triggered TG inflammation, with a vasoconstrictor (IS) or a neutral stimulator (CFA) there is no change in BBB passage, and (ii) the trigeminal ganglion is readily exposed to circulating molecules and could provide a site of antimigraine drug interaction with the trigeminal system.

OR15

The development of guanylate cyclase inhibitors for the treatment of migraine

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Background: The nitric oxide pathway has been heavily implicated in migraine, and the nitric oxide donor nitroglycerin (NTG) has been shown to reliably trigger migraine in humans. NTG stimulates soluble guanylate cyclase (sGC), the main NO receptor in the body, which increases production of cGMP. The guanylate cyclase pathway is of particular relevance in migraine as upregulation of cGMP by NTG or sildenafil (phosphodiesterase 5 inhibitor) produces headache but no other type of pain. Although NTG activates the sGC pathway, it also produces oxidative stress; and it is not entirely clear how these two events contribute to the pro-migraine effects of NTG. In an effort to determine the exact role of sGC in migraine we developed a novel sGC stimulator and inhibitor and tested these compounds for migraine-associated pain in mice.

Aim: The goal of this study is to determine the effectiveness of sGC inhibitors as novel anti-migraine therapies.

Methods: NTG, VL-102 (sGC stimulator), and/or RG212 (sGC inhibitor) were administered IP to male and female mice every second day for 9 days. On test days, basal and drug-evoked mechanical hypersensitivity was evaluated using von Frey hair stimulation.

Results: VL102-evoked acute and chronic mechanical hyperalgesia in a dose-dependent manner. This hyperalgesia was blocked by the migraine therapies sumatriptan and topiramate. Interestingly, the sGC inhibitor RG212 also inhibited acute and chronic hyperalgesia induced by VL102 and NTG.

Conclusions: These results verify that NTG causes migraine-related pain through activation of the sGC pathway, and that sGC inhibitors would be promising anti-migraine treatments.

OR16

Development of a reproducible target-engagement biomarker for TRPA1 antagonists

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Background: Among the transient receptor potential (TRP) channels, TRPA1 is emerging as a new target for the development of anti-migraine drugs. As activation of TRPA1 results in the release of pro-inflammatory neuropeptides, including calcitonin gene-related peptide, TRPA1 antagonists might have the potential to treat migraine. Peripheral TRPA1 activation can be induced by cinnamaldehyde (CA).

Aim: To develop a reproducible target-engagement biomarker for TRPA1 by activating the channels with local application of CA. Part 1: dose finding; Part 2: within-subject reproducibility based on concordance correlation coefficient (CCC).

Methods: Part 1: healthy subjects received topically 3%, 10%, and 30% CA at predefined sites on the volar surface of the right forearm. Part 2: subjects received topically two 10% CA doses during 2 visits separated by a washout period of at least 7 days. CA-induced changes in dermal blood flow (DBF) were assessed by laser Doppler perfusion imaging at 10, 20, 30, 40 and 50 minutes post-CA expressed as area under the curve from 0 to 30 minutes post-CA ($AUC_{0–30}$).

Results: Part 1: all doses of CA increased DBF ($n = 11$, $p < 0.05$, ANOVA), compared to placebo at all timepoints, with the maximum response at 10–20 min post-CA. Part 2: using 10% CA, arm-to-arm reproducibility was almost perfect ($n = 6$, CCC[J3] = 0.90); period-to-period reproducibility moderate ($n = 11$, CCC = 0.69). Based on sample size calculations, a sample size of 10 subjects is needed to detect a 30% shift between groups.

Conclusion: Cinnamaldehyde induces a reproducible within-subject increase in DBF. We provide a non-invasive model in humans to test TRPA1 antagonists.

OR17

Nitric oxide signalling in the A11 hypothalamic nucleus facilitates trigeminovascular activation

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Introduction: Dopaminergic mechanisms have been suggested to play a role in migraine. The hypothalamic A11 nucleus is pivotally the only nucleus that provides a dopamine-driven inhibitory effect on nociceptive transmission in the trigeminocervical complex (TCC). Nitric oxide (NO) donors suppress the firing rate of A11, suggesting the potential involvement of dopaminergic disinhibition at the level of the TCC.

Aims: To examine if local NO signalling in the A11 hypothalamic nucleus modulates the activity of second order neurons in the TCC.

Methods: The NO donor nitroprusside (SNP), or vehicle control (artificial CSF), were microinjected in the A11 nucleus of anaesthetised rats. Their effects were examined on the extracellular neuronal firing of second order neurons in the TCC, activated in response to stimulation of the middle meningeal artery. In a different group, animals were pre-treated with quinpirole, a D_2 receptor agonist, prior to SNP microinjection in the A11.

Results: Microinjection of SNP significantly facilitated spontaneous and evoked neuronal firing of second order neurons for at least 20 min ($P < 0.05$). Artificial CSF had no significant effects on the firing rate of second order neurons ($P = 0.28$). Pre-treatment with quinpirole, significantly blocked the SNP-induced facilitation of evoked neuronal activity corresponding to Aδ-fibres activation.

Conclusions: Our data suggest that disinhibition of dopaminergic transmission from the A11 nucleus may contribute to the development of migraine attacks following administration of nitric oxide donors. The D_2 receptor may present a therapeutic target for potential migraine treatments.

OR18

Susceptible genes of restless legs syndrome in migraine

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Objective: Several genetic variants were found to increase the risks of restless legs syndrome (RLS). Genetic factors for RLS have not been determined in migraine. The present study aimed to determine the genetic contributions underlying these two highly comorbid diseases.

Methods: Twelve single nucleotide polymorphisms (SNPs) at four RLS-risk genes, including *MEIS1*, *BTBD9*, *MAP2K5* and *PTPRD,* were genotyped in 210 migraine patients with RLS and 785 without RLS. Association analyses were performed in overall subjects and subgroups by stratifying the subjects into migraine with aura, migraine without aura, episodic migraine (EM) and chronic migraine (CM). Multivariate regression analyses were conducted to further verify genetic markers and environmental risk factors in relation to RLS in migraine.

Results: Among the four tested genes, only *MEIS1* was significantly associated with RLS. The most significant SNP rs2300478 at *MEIS1* increased the risk of RLS by 1.40-fold in overall migraine subjects ($p_{corr} = 0.0078$). Subgroup analyses found that *MEIS1* only augmented the risk of RLS in EM (odds ratio (OR) = 1.99, $p_{corr} = 0.0003$) but not in CM (OR = 0.93, $p_{corr} = 0.7$). Multivariate regression analyses showed that rs2300478 at *MEIS1* (OR = 1.37, p = 0.021), CM diagnosis (OR = 1.50, p = 0.029) and depression (OR = 1.78, p = 0.010) were independent predictors of RLS in migraine.

Conclusions: Our study confirmed that *MEIS1* variants were associated with RLS risks in migraine. Since the genetic function of *MEIS1* is modulation of ferritin production and iron transport, the imbalance of iron homeostasis and dopaminergic system might be implicated in the connection between RLS and migraine.

OR19

Altered gray matter volume and functional connectivity in "strict-criteria" tension-type headache

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Background: Migraine is associated with decreased gray matter volume (GMV) and altered brain connectivity, while pertinent studies in tension-type headache (TTH) are rare.

Aim: To investigate the structural and functional changes of the brain in patients with episodic (ETTH) and chronic TTH (CTTH)

Method: Consecutive patients with ETTH, CTTH and age- and sex-matched healthy controls were enrolled for brain MRI studies. Patients were excluded if they had coexistent migraine or any migrainous features for their headache. Changes of GMV associated with headache diagnosis and frequency were examined by voxel-based morphometry. The seed-based resting-state functional connectivity was subsequently investigated with the region of interest obtained from headache frequency-related GMV changes.

Results: Compared to the controls (n = 36), the patients with ETTH (40.4 ± 12.8y, n = 27) showed increased GMV in the anterior cingulate (ACC), superior frontal (SFG), middle frontal (MFG) and superior temporal gyri (STG). Patients with CTTH (42.6 ± 12.7y, n = 31) also showed increased GMV in SFG and the inferior parietal lobule. Moreover, GMV was increased in ETTH than in CTTH in the parahippocampal gyrus, ACC and insula. In all patients, the headache frequency was negatively correlated with the GMV of a subregion in ACC; functional connectivity with this seed was disrupted in precuneus for ETTH and additionally in SFG, MFG, STG and the head region of the primary somatosensory cortex for CTTH (all corrected $p < 0.05$).

Conclusion: TTH is associated with adaptive GMV increase, and the evolution from ETTH to CTTH is characterized by reduced GMV and connectivity of ACC.

OR20

Headache attributed to aereoplane travel keeps on flying: data from a series of 130 patients

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Introduction: Headache attributed to aereoplane travel (AH) indicates a new form of headache strictly related to airplane travel, whose attacks have peculiar features. Its diagnostic criteria have been codified in ICHD 3beta (1).

Methods: Following our previously published paper on 75 cases (2), we kept on receiving worldwide filled up questionnaires.

Results: Up to now, 130 cases (males: 59%) were studied. The pain site was mainly frontal-orbital (n = 105) or frontal-parietal (n = 9). A strictly unilateral side was reported in 84% of patients; side-shift in different attacks was observed in 21%. The mean age at onset was 35.7 years (range 7–63). AH attacks occurred during landing (in nine patients also during take-off), lasted less than 30 minutes and remitted spontaneously. Its intensity was very severe or severe. Only in 16 cases the first attack occurred during the first flight. The attacks presented in more than 50% of flights in 35 patients; 23 reported its occurrence during every flight. AH negatively affected the propensity to air travel in above 75% of the sufferers. Prophylactic use of NSAIDs prevented or effectively relieved the attacks in more than 50% of cases.

Conclusions: These new data confirm the stereotyped features of this specific headache, in keeping with the ICHD crieria. Considering the impact of AH, passengers should be appropriately informed about the existence of this severe headache, on its benign nature and its potential prevention.

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OR21

Corresponding increase of gray matter volume and brain metabolism in the visual association cortex in patients with visual snow syndrome

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Background: The Visual Snow syndrome (VS) is highly associated with comorbid migraine and typical migraine aura. It consists of a continuous and very disabling TV snow-like visual disturbance along with other visual symptoms. Hypermetabolism of the lingual gyrus has been shown recently in patients with VS (Schankin et al. Headache. 2014;54:957–66).

Aim: To investigate whether the brain metabolic alterations in VS translate to structural changes in another brain imaging modality.

Method: We used [18F]FDG-PET and structural T1-weighted MRI in 20 VS patients and 20 matched control subjects. Data were analyzed using SPM8 and the voxel-based morphometry toolbox VBM8.

Results: When compared to control subjects, VS patients showed hypermetabolism in the right lingual gyrus (BA 19) with corresponding gray matter volume increase in the nearby right fusiform gyrus. The additional areas of hypometabolism in the left inferior parietal lobule (BA 40) and right superior temporal gyrus (BA 22) were not associated with changes in gray matter volume in VBM.

Conclusion: The concordant increase of structural gray matter volume and brain metabolism in two different brain imaging modalities implicates a role for the visual association cortex in the generation or perception of VS. Migraineurs have a similar pattern of hypometabolism in the inferior parietal lobule and superior temporal gyrus supporting a pathophysiological overlap between migraine and VS.

OR22

Headache-related utilization of healthcare and acute medications among patients with medication overuse headache in europe and latin america. A descriptive, multinational, multicenter study (comoestas project)

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Background: Medication overuse headache (MOH) is a very costly disorder, both due indirect costs and due to medication and healthcare utilization.

Aim: To characterize headache-related healthcare utilization and acute medication overuse among patients with MOH in Europe and Latin America (LA).

Methods: This descriptive, cross-sectional, observational study included 669 patients with MOH referred to European and Latin American headache-centers. Information about acute medication and healthcare utilization were collected by extensive questionnaires, supplemented with structured interviews. Information about national healthcare systems was collected.

Results: More European patients (57%) compared with Latin American patients (27%) visited general practitioners ($p < 0.001$), and 83% of European patients compared to 38% in LA consulted headache specialists ($p < 0.001$). A total of 20% in Europe and 30% in LA visited the emergency room ($p = 0.007$). Triptans were overused by 31% patients in Europe and by 6% in LA ($p < 0.001$), whereas ergotamines were overused by 4% in Europe and 72% in LA ($p < 0.001$). Simple analgesics were overused by 54% in Europe and by 33% in Latin America ($p < 0.001$), while combination-analgesics were more equally overused (24% in Europe and 29% in LA).

Conclusion: There are marked international variations in healthcare utilization and in overuse of acute medications among patients with MOH. European patients have considerably more healthcare contacts than Latin American patients. Triptans are frequent causes of MOH in European but not in LA, where patients more often overuse ergotamines. Combination-analgesics and simple analgesics seem to be major causes of MOH globally. Focused prevention campaigns against MOH should be initiated.

OR23

Dynamic white matter hyperintense lesions in reversible cerebral vasoconstriction syndromes

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Background: White matter hyperintense lesions (WMH) have been reported in patients with reversible cerebral vasoconstriction syndromes (RCVS); however, their characteristics and biological meaning have not been explored.

Aim: To investigate the distribution and evolution of WMH in patients with RCVS.

Methods: Patients with RCVS were recruited and followed up with three-Dimensional (3D) CUBE Fluid-attenuated inversion recovery images (FLAIR) sequence with 1mm slice thickness using a 3-Tesla magnetic resonance (MR) machine. The FLAIR lesion segmentation toolbox (FLEX) was then used to segment WMH automatically. The brain was divided into 7 regions, including bilateral frontal, parietal, limbic, subcortical, temporal, and occipital lobes, as well as cerebellum. The WMH was parcellated into periventricular ($\leq$13 mm from ventricles) and deep ($>$13 mm from ventricles) WMH.

Results: Sixty patients with RCVS (7M/53F; average age 50.4 ± 9.4 years) finished the study with a total of 166 MRIs performed. The total volume of WMH was dynamic along the disease course, with a temporal trend similar to that of vasoconstrictions. The maximum volume was noted (7.2 ± 14.6 cm^3) at the 3rd week after headache onset, while the lowest volume was noted at the 4th week (0.8 ± 0.6 cm^3). WMH were predominantly periventricular during the first two weeks, and evolved to predominantly deep WMH in the 3rd week. Most of the WMH were located at the frontal area. No clinical parameters were associated with loads of WMH.

Conclusion: WMH in RCVS waxed and waned in a pattern similar to the temporal evolution of vasoconstrictions. The clinical significance remained to be determined.

PO001

Migraine acute therapy

The effects of wet-cupping on intensity o f headache in migraine sufferers

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Introduction: Migraine has a collection of symptoms characterized by recurrent and severe headaches. Complementary methods can reduce the use of analgesics and might be effective in reducing pain in patients waiting for analgesics. The purpose of this study was to determine the effect of wet-cupping on patients within 20 to 60 years of age diagnosed with migraine headaches.

Migraine has a collection of symptoms characterized by recurrent and severe headaches. Complementary methods can reduce the use of analgesics and might be effective in reducing pain in patients waiting for analgesics. The purpose of this study was to determine the effect of wet-cupping on patients within 20 to 60 years of age diagnosed with migraine headaches.

Materials & Methods: This study was carried out before and after clinical trial; the samples were 47 patients diagnosed with migraine headaches. Inclusion criteria consisted of a confirmed diagnosis of migraine and all the patients had to be 20 years old or above. The pain severity was evaluated twice; at the beginning and after 14 days following two sessions of wet cupping with an interval of 2 weeks. The visual pain scale was evaluated in the patients. Data were analyzed by paired t-test and Fisher's exact test using SPSS, version 17, the acceptable criterion was chosen as below 0.05.

Results: The means for pain intensity at the beginning and the end of the study were significantly decreased ($P = 0.001$). In most patients pain was intolerable before wet-cupping (averagely 7.79%), however, after the first (53.1%) and second (48.9%) sessions of wet-cupping, pain respectively lessened (3.15%). The mean of pain reduction in women was more than in men, but the difference was not significant.

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Conclusion: Findings of the research indicates that using wet-cupping as a complementary method can influence the intensity of migraine pains.

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PO002

Migraine acute therapy

Neuronal survival by carbamazepine on cortical spreading depression in rats

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Background: Spreading depression characterized by negative DC deflection, followed by isoelectricity phase, electrophysiological recording used as standard test to confirm SD initiation refers to waves of mass cellular depolarization associated with distribution of ion and water. Correlations of SD by in pathophysiology of various neurodegenerative disorder including Epilepsy, ischemia, stroke and migraine have been reported. We also indicated that, two consecutive KCl injections could trigger cell death cascade. Clinical studies reported neuronal loss in patients who suffer from migraine.

Aim: Both activation of Na^+ channel current induced action potentials and NMDA-controlled ion channels are involved in pathophysiology of SD. Carbamazepine is known as Na^+ channel blockader and widely use in treatment of epilepsy.

Methods: In the present study, 36 Wistar rats received systemic Carbamazepine as before induction of SD by inracerebral induction of KCl to investigate the role of sodium channelsin SD phenomenon, T-maze behavioural test followed by histological assessment were done on Hippocampus region.

Results: Our histological assessment revealed a significant reduction in mean number of necrotic and apoptotic cell in the hippocampal region. T-maze test revealed that sodium

channel blockade could reduce SD induced memory impairment.

Conclusion: We conclude that neuronal firing after glutamate activation play critical role in SD wave initiation and propagation. Therefore blocking sodium channels attenuated the neurological and behavioural effects of SD. Blockade of Na+ channel could interfere with CSD, and may have efficacy as a therapeutic agent for related neurological disorders such as epilepsy.

PO003

Migraine acute therapy

Greater occipital nerve blockade for the treatment of prolonged or persistent aura: a pilot study

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Background: Lamotrigine has been found to be effective for the prevention of migraine aura. However, there are no proven therapies for the acute treatment of prolonged (>1 hour) or persistent (>1 week) migraine aura.

Aim: To assess the effectiveness of greater occipital nerve (GON) blockade as a symptomatic treatment for long-lasting (prolonged or persistent) migraine aura.

Methods: A non-controlled clinical trial was performed at the Headache Unit and the Emergency Department of a tertiary hospital from May 2013 to April 2014. Patients with prior diagnosis of migraine with aura who presented with aura lasting >2 hours were consecutively recruited. All patients underwent a bilateral anaesthetic blockade of the GON with bupivacaine 0.5%. Follow-up lasted 24 hours.

Results: A total of 22 auras were treated in 18 patients (16 women and 2 men, mean age 43.9, range 16 to 61 years); 4 patients were treated on 2 different episodes. Auras consisted of visual (n = 13), visual plus sensory (n = 4), or sensory symptoms (n = 5). Eleven patients met diagnostic criteria for persistent aura without infarction. The response was complete without early recurrence in 11 cases, complete with early recurrence in 2 cases, and partial (>50% improvement) in 6 cases. Complete responses without recurrence were less common in cases with persistent aura (3 out of 11 compared to 8 out of 11 in the remaining cases; chi-square test, $p = 0.033$).

Conclusions: GON blockade is emerging as an effective symptomatic treatment for prolonged or persistent migraine aura. Randomized controlled trials are still required to confirm these results.

PO004

Migraine acute therapy

Therapeutic effect of intranasal evaporative cooling in patients with migraine. A report of the results of the cool head i pilot study

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Background: Studies have previously demonstrated effectiveness of a variety of cryotherapy approaches in migraine. Intranasal evaporative cooling due to vascular anatomy, allows the transfer of venous blood from nasal and paranasal mucous membranes to the dura mater, providing an excellent anatomical basis for the cooling processes.

Aim: The aim of this study was to ascertain whether intranasal evaporative cooling may be an effective intervention in an acute migraine attack.

Methods: We conducted a prospective, open-label, observational, pilot study. Twenty-eight patients who satisfied the ICHD-2 diagnostic criteria for migraine were recruited. A total of 20 treatments were administered in 15 patients. All patients provided pain and migraine-associated symptoms severity scores.

Results: Out of the 20 treatments, immediately after the treatment, 8 treatments (40%) resulted in pain and symptoms freedom, while a further 10 treatments (50%) resulted in partial pain and symptoms relief. At 2 hours, 9 treatments (45%) provided pain and symptoms freedom, with a further 9 treatments (45%) resulting in partial pain and symptoms relief. At 24 hours, 10 treatments (50%) resulted in pain and symptom freedom and 3 (15%) provided partial pain relief. In summary 13 patients (87%) had benefit from the treatment within 2 hours that was sustained at 24 hours.

Conclusions: This pilot study showed that intranasal evaporative cooling was safe and gave considerable benefit to patients with migraine, improving headache severity and migraine-associated symptoms. An adequately powered randomised controlled study will be required to confirm the potential of this application in the management of migraine.

PO005

Migraine acute therapy

Inpatient management of refractory headache in egypt. The first patient

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Background: To the best of our knowledge, inpatient treatment practice has started in Egypt in 2014. Taking into consideration the reduced awareness and the limited medical choices (No IV DHE, SC Sumatriptan, among others), we present the first case who went through our inpatient program.

A 38 years old Physics university lecturer, type A personality, had chronic migraine with medication overuse(NSAIDS, ASA) and occipito-temporal allodynia. He had 12 disabling migraine attacks last month. His last headache free day was 12 years ago. He tried Amitriptyline, Topiramate, Cidamex (CSF opening pressure 27, no other manifestations of IIH). All had a limited effect. Dose escalation was difficult due to side effects. He received IV domperidone, dexamethasone, oral promethazine, ranitidine and fluids for 3 days with partial improvement. Xylocaine IV infusion was added for 48 hours and he became headache free. Upon discharge he received Botox and was maintained on Propranolol, Duloxetine, and Levetiracetam. During the next 12 weeks, he had around 2–3 headache free days per week, 4–5 migraine attacks per month with extra work loads or poor sleep. He can tolerate the headaches at a 1–3 intensity in the rest of the days. He received his second Botox, anxiolytic was added, and behavioral management options discussed. He is preparing to travel for a postdoc fellowship.

Conclusion: This highly educated person was aware of his problems and accepted the treatment options that other cases declined. Awareness about headache types and available management options should increase in Africa and the Middle East.

PO006

Migraine acute therapy

An example of insufficient reporting of tolerability problems in reviews of an anti-migraine drug (the 5HT1F receptor agonist lasmiditan)

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Background: Better reporting of adverse events (AEs) are neededin original study papers and the widely read reviews on drugs. In a review from2012 on efficacy and AEs after oral lasmiditan in a pivotal phase II trial wedescribed AEs as mostly moderate (40%) or severe (27%).

Aim: The aim of this mini-review was to evaluate how this statement was cited insubsequent reviews from 2012 to 2014.

Methods: Papers citing the original review were found in Google Scholar.

Results: A total of 14 references were found and 9 reviews were evaluated. Inonly 2 of 9 reviews was it mentioned that AEs after lasmiditan are a problemand that most AEs are moderate or severe.

Conclusion: The insufficient reporting of AEs observed in thismini-review could be due to a tendency among authors oftherapy reviews in migraine to stress positive results of efficacy and todownplay AEs problem. This is not in the interest of our patients who needsober information about drugs.

In contrast, it is likely that pharmaceutical industryand investors are not any longer interested in lasmiditan since nothing hasbeen heard of the drug for the last 2 years. A likely reason is the manyproblematic AEs in the pivotal phase II trial.

PO007

Migraine acute therapy

Sensitive premonitory symptoms and unilateral pain predict the response to frovatriptan in migraine attacks

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Background: Some characteristics of the migraine attack (i.e. severe headache pain, presence of photophobia/phonophobia and presence of nausea) have been associated with response to triptan, although not all the features, such as premonitory symptoms, have been investigated specifically with a prospective study.

Aim: To evaluate the association between clinical characteristics of migraine attack and efficacy of frovatriptan 2.5 mg po.

Methods: We prospectively recruited thirty consecutive patients affected by migraine without aura at the Headache Center of "Mondino" Institute of Pavia. Each patient had to record in a diary the features of three consecutive migraine attacks at the moment of frovatriptan intake. Data inquired were: pain intensity, unilateral location, pulsating quality, presence of nausea, vomiting, photophobia, phonophobia, osmophobia, allodynia, cranial autonomic symptoms, premonitory symptoms, delay of the triptan intake from the onset of pain, and intensity of pain two hours after triptan intake.

Results: Data were complete for 86 attacks. Of these, in 30 attacks (34%) patients were pain free at 2 hours after medication intake (PF). In the univariate analysis the only feature associated with PF was unilateral pain ($P = 0.006$). In the stepwise multivariate analysis, delay of triptan intake (OR 1.008, 95% CI 1.001–1.015, $P = 0.034$), unilateral pain (OR 19.93, 95% CI 3.31–126.67, $P = 0.002$), and presence of photophobia and/or phonophobia and/or osmophobia in the premonitory phase (OR 31.97, 95% CI 3.22–317.00, $P = 0.003$) were found as independent predictors of PF (table).

Conclusion: Sensitive premonitory symptoms and unilaterality of pain are strongly associated with response to frovatriptan.

PO008

Migraine acute therapy

Treatment of migraine should be evidence-based also when recommended by health authorities and in textbooks

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Background: We found this FDA prescription information for oralsumatriptan: "If the headache returns or ifthe patient has only partial response, the dose may be repeated after 2 hours, for a maximum of 200 mg in a 24-hour period". Incontrast, 2 randomized, controlled trials (RCTs) have shown no effectof a second dose of sumatriptan.

Aim: We wanted to evaluate whether this peculiar recommendation of a second dose ofa triptan was a more general phenomenon in the USthan in Europe or Canada.

Methods: We reviewed the FDAprescription of triptans, two recent US textbooks on neurology, Europeanand Canadian migraine treatment guidelines.

Results: The use of a second dose for efficacy is recommended in the FDAapproved prescribing information for sumatriptan, naratriptan, andzolmitriptan, but not for rizatriptan, almotriptan. eletriptan andfrovatriptan.

In one USextbook it is stated concerning triptan tablets: "They should be administeredin their optimum doses and may be repeated every 2 hours (for naratriptan every4 hours), until headache is relieved or the maximum daily dose is reached."

The European and Canadian guidelines discouragethe use of a second dose when the first dose is ineffective.

Conclusion: The FDA recommendation of a second dose of severaloral triptans is an enigma.

PO009

Migraine acute therapy

Noninvasive vagus nerve stimulation for acute treatment of high-frequency and chronic migraine: an open-label study

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Background: We evaluated the effects of acute noninvasive vagus nerve stimulation (nVNS) in patients with high-frequency episodic migraine (HFEM) or chronic migraine (CM).

Methods: Open-label, single-arm, multicenter, study. Patients with HFEM or CM self-treated up to 3 consecutive mild or moderate migraine attacks occurring in a 2-week period by delivering two 90-second doses of nVNS, at 3-minute intervals to the right cervical branch of the vagus nerve.

The primary endpoint was pain freedom at 2 hours. Secondary endpoints were pain relief at 1 and 2 hours, pain freedom at 1 hour, absence of nausea, photophobia, and phonophobia at 2 hours, complete recovery from functional disability at 2 hours, use of rescue medications, safety, tolerability and patients satisfaction.

Results: Of the 50 migraineurs enrolled (CM/HFEM: 36/14), 48 treated 130 attacks. Headache response was 45.8% at 1 hour and 60.4% at 2 hours, whereas freedom from pain was 22.9% at 1 hour and 33.3% at 2 hours (n = 48). When considering all attacks (n = 130), pain free was 17.7% at 1 hours and 23.1% at 2 hours, whereas pain relief was 21.5% at 1 hour and 34.6% at 2 hours.

Freedom from nausea at 2 hours occurred in 30.6% of attacks, from photophobia in 27.3%, and from phonophobia in 62.5%. Complete recovery from functional disability at 2 hours occurred in 35.3% of attacks. Rescue medications were taken by 56.3% of patients. nVNS was well tolerated; 45.8% of migraineurs were satisfied with nVNS.

Conclusions: nVNS may be an effective acute treatment for HFEM or CM.

PO010

Migraine acute therapy

Reduced efficacy of sumatriptan in migraine with aura vs. Without aura

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Objective: To determine if acute migraine treatment outcome is different in migraine with aura compared with migraine without aura.

Methods: We examined pooled outcome data for sumatriptan treatment of migraine with and without aura from the sumatriptan-naratriptan aggregate patient (SNAP) database. We also examined similar outcome data for inhaled dihydroergotamine (DHE) from a single large randomized controlled study.

Results: The pooled pain free rates 2 h post-dose for sumatriptan 100 mg were significantly higher in patients treating attacks without aura (32%), compared to the group who treated attacks with aura (24%),($P < 0.001$). The NNT for 2 h pain free was 4.4 for attacks without aura and 6.2 for attacks with aura. For the clinical trial of DHE, the 2 h pain free rates did not differ between patients treating attacks without aura (29.4%) compared to those who treated attacks with aura (27.2%; $P = 0.65$). The NNT for 2 h pain free was 5.8 for attacks without aura and 5.0 for attacks with aura.

Conclusion: This post-hoc analysis of pooled data from multiple randomized trials indicates that sumatriptan is less effective as acute therapy for migraine attacks with aura compared to attacks without aura. In the single study of inhaled DHE, the treatment had similar efficacy for migraine attacks with and without aura. Different responses of migraine with vs. without aura to acute therapies may provide insight into underlying migraine mechanisms and influence the choice of acute therapies for different types of migraine attacks.

PO011

Migraine acute therapy

Inhibition of monoacylglycerol lipase activity modulates the activation of brain structures relevant for migraine pathogenesis

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Background: Experimental evidence shows that the antinociceptive action of endocannabinoids, related to the modulation of the trigeminovascular system activity, may be helpful for prompting new targets for the treatment of

migraine. URB602 is an inhibitor of monoacylglycerol lipase (MAGL), a key enzyme in the hydrolysis of the endocannabinoid 2-arachidonoylglycerol. URB602 induces analgesia in animal models of pain not related to migraine, but there is no pre-clinical information as regards its potential effect in migraine pain.

Aim: To evaluate whether URB602 administration interferes with the level of activation of brain structures involved in migraine.

Methods: Nitroglycerin (NTG) induces neuronal activation in a specific subset of brain nuclei that are considered relevant for the development of migraine attacks. In this study we evaluated the changes caused by URB602 in NTG-induced neuronal activation

Male Sprague Dawley rats were treated with NTG (10 mg/kg, i.p.) followed by URB602 (2 mg/kg, i.p.) or vehicle (DMSO, 1 ml/kg, i.p.). Their brain were processed for the detection of c-Fos protein, used as a marker of neuronal activation.

Results: Brain mapping of nuclei activated by NTG administration showed that MAGL inhibition significantly reduced neuronal activation in the following areas: nucleus trigeminalis caudalis, area postrema, nucleus tractus solitarius, ventrolateral column of the periaqueductal grey, locus coeruleus and parabrachial nucleus.

Conclusion: The inhibition of MAGL activity, with the theoretical increase of central content of 2-arachidonoylglycerol, may modulate the activation of structures involved in pain perception and pain integration in an animal model specific for migraine.

PO012

Migraine acute therapy

Anticephalgic photoprotective premedicated mask: a report of a successful study of a treatment for migraine and/or tension headaches

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Objective: Thisstudy was performed to determine the efficacy of an anticephalgicphotoprotective mask in conjunction with a topical medication containingbryonia and rhus toxicodendron in the treatment of migraine and/or tensionheadache.

Methods: Thirty-three patients were given masks and tubes of topicalmedication containing the bryonia and rhus toxicodendron. They were instructedto apply the medication to their frontalis and/or temporalis regions in theevent they should suffer a headache and apply a photoprotective mask. Furthermore, they were instructed to take their usual oral or parenteralmedications if required for the relief of the headache. They subsequentlyfilled out forms rating the degree of relief which they attributed to the topicalmedication and the mask using a 0–10 scale. At the interview following thecompletion of their participation in the study, the patients were also simplyasked if this form of treatment helped or not.

Results: Thirty out of 33 patients stated the medication and the maskwere effective over and above the normal degree of relief they were receivingfrom their oral and/or parenteral medications. This study demonstrated asignificant efficacy rate (91%) in the treatment of migraine and/or tensionheadache with the anticephalgic mask in conjunction with a topical creamcontaining bryonia and rhus toxicodendron.

Interpretations: This study demonstrated a significant efficacy rate inthe treatment of migraine and/or tension headache with the anticephalgic maskin conjunction with a topical cream containing bryonia and rhus toxicodendron.

PO013

Migraine acute therapy

Efficacy of occipital nerve block in patients suffering from occipital neuralgia

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Background: Occipital neuralgia (ON) can be a debilitating illness, for which optimal treatment strategies have not been well studied.

Aim: To assess the efficacy of occipital nerve block (ONB) using injected steroids in patients who suffer from ON.

Methods: A retrospective study of adults with ON treated over a 5 year period was undertaken. Patients who

received at least one ONB and attended at least one follow-up visit were included. A 10-point numeric scale was used to assess patient response. Response to ONB was defined as follows: 'poor' 0–3 point improvement; 'good' 4–6 point improvement; 'very good' 7–10 point improvement.

Results[FM1]: 562 patients met inclusion criteria. 423 were female (75%). Mean age was 58.6 +/− 16.7 years. 458 out of the overall group rated their response to ONB as good or very good (82%). 323 patients were treated previously with medical management alone. Of this group, 261 (81%) had a good or very good response. 194 patients received a combination of treatments including medications, physical therapy and acupuncture. Of this combined therapy group, 161 (83%) had a good or very good response. 44 patients received no prior therapy and of this group 35 (80%) had a good or very good response. ONB was equally effective across both genders and all age groups.

Conclusions: In a large retrospective study of 562 patients with occipital neuralgia, occipital nerve block as sole treatment or after other failed treatment strategies was highly successful, resulting in a response rate of 80% or higher.

PO014

Migraine acute therapy

Total migraine freedom for breath powered intranasal delivery of 22mg sumatriptan powder (AVP-825) versus 100mg oral sumatriptan from the compass study in acute migraine

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Background: Migraine-associated symptoms—nausea, photophobia, phonophobia—can contribute to disability and direct healthcare costs. The composite efficacy endpoint Total Migraine Freedom (TMF) assesses freedom from pain and migraine-associated symptoms, providing a more comprehensive understanding of treatment impact than evaluation of items individually.

Aim: TMF was assessed for AVP-825, an investigational Breath Powered intranasal delivery system (22 mg sumatriptan powder), vs 100 mg oral sumatriptan (oral-SUM) in COMPASS (NCT01667679).

Methods: Multicenter crossover study with two 12-week double-blind periods. Patients (2–8 attacks/month) were randomized to AVP-825 plus oral placebo or identical placebo delivery system plus 100 mg oral-SUM (period-1); treatment switched for period-2. Patients treated $\leq$5 qualifying migraines/period (<1 hour from onset, even if mild). Percentage of attacks with TMF (pain freedom and absence of migraine-associated symptoms, including vomiting) 10 minutes–2 hours post-dose was calculated *post hoc* and compared (Chi-square test).

Results: 185 patients treated migraines in both periods, yielding 1531 migraines (765 AVP-825, 766 oral-SUM). TMF rate was significantly greater with AVP-825 vs oral-SUM at all timepoints from 15–90 minutes: 15-minutes (7.2% vs 3.7%; $P<.01$), 30-minutes (18.0% vs 10.8%; $P<.001$), 45-minutes (30.7% vs 21.4%; $P<.001$), 60-minutes (40.9% vs 33.3%; $P<.01$), 90-minutes (52.7% vs 45.6%; $P<.01$). At 2 hours, TMF rates did not differ significantly (60.6% AVP-825 vs 56.7% oral-SUM; $P=.11$).

Conclusion: AVP-825 treatment results in higher TMF rates at earlier timepoints than the most efficacious dose of oral-SUM, despite delivering much less drug. These results are consistent with the other COMPASS outcomes and indicate AVP-825 has superior early efficacy vs oral-SUM.

PO015

Migraine acute therapy

Consistency of response in the compass study [breath powered intranasal delivery of 22mg sumatriptan powder (AVP-825) versus 100mg oral sumatriptan in acute migraine

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Background: AVP-825 is an investigational product, which provides novel Breath Powered™ intranasal delivery of low-dose sumatriptan powder (22 mg). AVP-825 showed significantly greater early efficacy vs 100 mg oral sumatriptan (oral-SUM) in COMPASS (NCT01667679).

Aim: Since consistent efficacy across multiple migraines is a priority among patients, early pain response across migraines was evaluated in COMPASS.

Methods: Multicenter, double-dummy, crossover with two 12-week double-blind periods. Patients received AVP-825 or 100 mg oral-SUM plus complimentary placeboes (period-1) then switched (period-2). Patients treated ≤5 qualifying migraines/period (<1 hour from onset, even if mild). Pain relief/freedom rates were calculated for the first 2 attacks, ≥2 of the first 3 attacks, and 3 of the first 3 attacks in each period, and compared using McNemar's test.

Results: For patients treating ≥2 attacks each period (n = 165 each group), AVP-825 was superior to oral-SUM in rate of pain relief (37.6% vs 18.8%, $P < .0001$) and pain freedom (10.9% vs 3.0%, $P = .0072$) at 30-minutes post-dose for the first two attacks. For patients treating ≥3 attacks each period (n = 140 each group), AVP-825 was superior to oral-SUM at 30-minutes post-dose for pain relief (51.4% vs 33.6%, $P = .0002$) and pain freedom (15.7% vs 6.4%, $P = .015$) in ≥2 of the first 3 migraines, and for pain relief (27.1% vs 12.1%, $P = .0002$) at 30-minutes post-dose in 3 of the first 3 migraines.

Conclusion: AVP-825 (22 mg sumatriptan nasal powder) resulted in more consistent pain freedom/relief across multiple migraines within 30 minutes vs 100 mg oral-SUM. Consistent rapid relief suggests the pharmacokinetic advantage of Breath Powered delivery of sumatriptan powder.

PO016

Migraine acute therapy

A survey of patient perceptions of non-invasive vagus nerve stimulation (NVNS) therapy for acute migraine attacks

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Background: Two years of experience with non-invasive vagus nerve stimulation (nVNS; gammaCore®) at our center indicates that nVNS is effective in the treatment of acute migraine attacks. Literature suggests that treatment persistence is a key determinant of the long-term efficacy of nVNS. We conducted a survey to assess patients' rationale for initiation and maintenance of nVNS therapy.

Aim: To investigate reasons for initiation and continued use of nVNS as abortive therapy for migraine attacks.

Methods: Patients who previously received nVNS and those currently receiving nVNS therapy for acute migraine attacks were surveyed. Reasons for initiating nVNS therapy and the reasons for continuing to administer nVNS therapy for acute migraine attacks were documented.

Results: Forty-nine of 60 patients who received survey questionnaires responded. Most patients were female (36 of 49 [73.5%]); mean age (SD) was 40.3 (10.5) years (range, 21–60 years). Among the 49 survey responders, reasons for initiation of nVNS therapy were resistance to standard migraine therapy (67.3%), previous drug-related side effects (55.2%), desire to try a nonpharmacologic therapy (45%), and confidence in the prescribing physician (51%). Reasons for continuing nVNS therapy were efficacy (69.5%), ease of use (65.5%), convenience (49.3%), few side effects (30.5%), confidence in the prescribing physician (40.8%), and curiosity regarding a novel treatment approach (26.7%).

Conclusion: Our survey on nVNS therapy initiation and continuation reflects patients' interest in novel treatment options for acute migraine attacks, and demonstrates that treatment efficacy is the primary motive for continuation of nVNS therapy.

PO017

Migraine acute therapy

Efficacy and tolerability of sumatriptan and paracetamol combination for the acute treatment of migraine

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Background: It is important to optimize the treatment of acute migraine attacks in order to provide fast relief and restauration of function. Migraine is known to be a multimechanistic neurovascular disorder. It has been established that adding Naproxen Sodium 500mg to Sumatriptan 85 mg improves clinical benefit over monotherapy. However, patients with contraindication or poor tolerability to NSAIDs are to avoid this combination.

Objective: To evaluate the efficacy and tolerability of a combination of Paracetamol 500 mg with Sumatriptan 100 mg as an abortive therapy for acute migraine attack.

Methods: Twelve patients with incomplete response or high recurrence rate after taking Sumatriptan monotherapy and a contraindication or intolerance to NSAIDs were instructed to treat three attacks each with a different therapy including the combination of Sumatriptan 100 mg with Paracetamol 500 mg, Sumatriptan 100 mg as monotherapy or Paracetamol 500 mg as monotherapy and record response. The patients were asked to treat with

monotherapy or combination therapy within the first twenty minutes after the onset of the attack.

Results: Response to the combination of Sumatriptan 100 mg and Paracetamol 500 mg was 77% after two hours compared with 51% after sumatriptan monotherapy and 44% after Paracetamol monotherapy. Tolerability was excellent in both, monotherapy and combination therapy. In particular, no symptoms of gastric irritation.

Conclusions: The combination of Sumatriptan 100 mg and Paracetamol 500 mg was more effective than monotherapy. Given the evidence of the multimechanistic nature of migraine, this combination should be considered on those patients on whom NSAIDs cannot be used and merits further investigation.

PO018

Migraine acute therapy

Use of single pulse TMS (STMS) to treat migraine with medication overuse

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Background: Addressing the overuse of acute medicines is a challenging but crucial component of migraine treatment in clinical practice. sTMS has previously shown efficacy in reducing migraine symptoms and acute medicines in the UK pilot programme.

Aim: To explore the utility of sTMS to treat migraine with acute medication overuse.

Method: Patients ($n = 28$) were selected by their Neurologist in open clinical practice and advised to reduce their intake of acute medicines. Headache nurses provided treatment instructions and collected baseline and outcome data through telephone surveys at Baseline, 6- and 12- week time points. The patients were instructed to treat with sTMS twice daily and acutely at attack onset, using the sTMS Medical Advisory Board (TMS-MAB) guidelines. Patients were encouraged to reduce acute medicines during the treatment period; a rate of reduction was not stipulated.

Results: Twenty-eight patients were prescribed sTMS and treated for 12 weeks. Of these: 86% ($n = 24$) reported a reduction in the number of days of acute medicine use, with 75% ($n = 21$) reporting reduced pain severity. Nineteen patients (68%) reported reduced migraine days and 15 (54%) had shorter attack duration. In addition, headache disability scores (HIT-6) were improved in 75% of patients ($n = 21$). The treatment was well tolerated and no adverse events were reported.

Conclusion: sTMS may be an effective bridge treatment for patients with medication overuse. The majority of patients reduced acute treatments and reported efficacy for migraine symptoms.

PO019

Migraine acute therapy

Concomitant administration of alprazolam and ibuprofen in acute migraine headache

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Since different factors are involved in migraine incidence and its triggers, a wide variety of drugs are used to manage of migraine. Combination therapy has shown its efficiency in treating migraine. In this study, we have taken the combination of ibuprofen and alprazolam as a probable efficient compound in reducing these headaches.

90 migraine patients were allocated in3 groups of 30, with an average of 2–6 attacks in month underwent. These three groups were unified by age, gender and their drug histories.tTe first group were given a single dose of ibuprofen 200 mg, the second group were given a single dose of ibuprofen 400 mg and the third group were given a single dose of ibuprofen 200 mg in companion with alprazolam 0.5 mg. Headache severity, functional disability and associated symptoms of the patients were recorded before and two hours after taking each regimen and were graded from 0–3 points. In all 3 groups, the severity of the headaches were reduced significantly after the course of drug therapy with 36% of reduction in the first group, 46% in the second group, and 74% in the third group, respectively ($p < 0.0001$). In the first group, nausea and vomiting were reduced from 92.3% to 22.3%, the second group from 96.7% to 13.3% and, finally the third group from 100% to 3.3% ($p < 0.0001$). In addition,

a significant reduction in photophobia and phonophobia was seen before and after taking the drugs ($p < 0.0001$).

The combination of ibuprofen200mg and alprazolam0.5 mg had significantly reduced the severity of the migraine headaches.

PO020

Migraine acute therapy

Delivery outcomes after acute migraine treatment in pregnancy: a retrospective study

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Background: Seeking acute care for migraine during pregnancy may be a marker of particularly severe and active disease. Data regarding acute treatment of such a population and their birth outcomes is lacking.

Aim: To describe therapies employed and subsequent birth outcomes in pregnant patients presenting with acute severe migraine in a hospital setting.

Method: Consecutive inpatient neurology consultations for acute severe headache in pregnant women at an urban, tertiary hospital over a 5 year period were reviewed.

Results: We identified 90 pregnant women with acute migraine free of secondary headache at initial presentation, including preeclampsia. The mean age was 29.3 years. Most patients were African American (38.9%) or Hispanic (34.4%), multiparous (70.0%) and presented in the 3rd trimester (50.0%). Diagnoses included migraine with aura (11.6%), migraine without aura (59.3%) and both (29.1%). A minority had chronic migraine (12.8%), and 31.4% presented in status migrainosus. Most patients (62.2%) were treated with a combination of oral and intravenous therapies, including oral acetaminophen (75.6%), intravenous metoclopramide and diphenhydramine (both 54.4%). Duration to delivery after acute presentation averaged 61.1 days. Rates of preterm deliveries were 40.0% and Cesarean deliveries were 39.9%. Though 16.7% ultimately developed preeclampsia, 53.3% were complicated with severe features.

Conclusions: Pregnant women seeking acute migraine treatment were exposed to a variety of medications, and experienced higher rates of Cesarean deliveries, preterm deliveries and preeclampsia than the general population. Though prospective studies stratified by degree of migraine severity are warranted, pregnancies in such patients should be considered high risk.

PO021

Migraine acute therapy

Long term efficacy of fascia-lysis technique combines with bone decompression technique in management of primary headache

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Primary headaches are "idiopathic"–occurring for no obvious reason,not the result of any underlying disease or process. Till now,primary headaches have many different possible treatments,but none proved to have long term efficacy. We are using a type of minimal invasive technique which is also the integration of Western & Chinese medicine. The aims is to lysis off the degenarated or thickening fascia which contributes to the adherance & compression of focal nerve & blood vessels,this can be achieved by using the Fascia-Lysis needle. In combination with Bone Decompression needle,we can further promotes the microcirculations of the related skull bone. Clinically,long term efficacy results can be gained by using the combination methods of Fascia-Lysis Technique & Bone Decompression Technique in Primary Headaches management.

PO022

Migraine acute therapy

Toll like receptor-3 agonist modulate immune response in cortical spreading depression model

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Toll like receptor-3 agonist modulate immune response in cortical spreading depression model

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Aims: Cortical spreading depression (CSD) is known to influence the expression of inflammatory genes. Toll-like receptors (TLR) are master regulators of innate immune function and involved in the activation of inflammatory responses in the brain. TLR3 agonist poly I:C exerts anti-inflammatory effect and prevents cell injury in the brain.

Methods: We examine the effect of systemic administration of poly I:C on the release of cytokines (TNF-α, IFN-γ, IL-4, TGF-β1, and GM-CSF) in the brain and spleen, splenic lymphocyte proliferation after induction of repetitive CSD in juvenile rats. Results: Poly I:C significantly attenuated CSD-induced production of TNF-α and IFN-γ in the brain as well as TNF-α and IL-4 in the spleen. Poly I:C did not affect enhancement of splenic lymphocyte proliferation after CSD. In addition, poly I:C significantly prevented production of CSD-induced dark neurons.

Conclusion: The data indicate neuroprotective and anti-inflammatory effects of TLR3 activation on CSD-induced neuroinflammation. Targeting TLR3 may provide a novel strategy for developing new treatments for CSD-related neurological disorders.

Keywords: Spreading Depolarization, Migraine, Immunotherapy, Neuroprotection, inflammation

PO023

Migraine acute therapy

Pharmacological profile of the tachycardic and vasopressor responses produced by (S)-isometheptene and (R)-isometheptene* in pithed rats

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Background: Isometheptene is effective in the acute treatment of migraine and tension-type headaches. It is composed of two stereoisomers (S and R), with different pharmacological properties.

Aim: This study investigated in pithed rats the cardiovascular effects by (S)-isometheptene and (R)-isometheptene as well as the pharmacological profile of the more potent vasoactive stereoisomer.

Methods: The effects of i.v. injections (0.03–10 mg/kg) of (S)-isometheptene or (R)-isometheptene on heart rate and blood pressure were analyzed in control experiments. The stereoisomer producing more pronounced tachycardic and/or vasopressor responses was further analyzed in rats treated intravenously with prazosin (0.1 mg/kg), rauwolscine (0.3 mg/kg), propranolol (1 mg/kg) or intraperitoneal reserpine (5 mg/kg, −24 h). Experiments were approved by our institutional ethics committee, in accord with National Institutes of Health guidelines.

Results: Compared with (R)-isometheptene, (S)-isometheptene produced greater vasopressor responses, whilst both compounds equipotently increased heart rate. The tachycardic response to (S)-isometheptene was abolished after propranolol, but remained unaffected by the other compounds. In contrast, the vasopressor responses to (S)-isometheptene were abolished after prazosin. Interestingly, after reserpine, the tachycardic response to (S)-isometheptene was abolished, whereas its vasopressor responses were attenuated and subsequently abolished by prazosin.

Conclusion: While the tachycardic response to (R)-isometheptene and (S)-isometheptene is similar, (S)-isometheptene produces greater vasopressor responses. The tachycardic response to (S)-isometheptene involves a tyramine-like action, whilst its vasopressor response involves both a tyramine-like action and a direct stimulation of alpha$_1$-adrenoceptors.

* (R)-isometheptene is being investigated in the US for tension-type headache under a US IND and is not approved for any indication.

PO024

Migraine acute therapy

Intravenous ketamine for the subacute treatment of refractory chronic migraine: case series

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Background and aim: Refractory chronic migraine is a challenging condition with great impact on individuals and society. Intravenous ketamine has been used to treat various refractory pain conditions. We aimed to present refractory migraine patients treated with intravenous ketamine in the hospital setting.

Methods: We reviewed charts of patients with chronic migraine refractory to multiple treatments, admitted to Mount Sinai Beth Israel Hospital from 2010 until 2014 for IV ketamine. A total of 6 eligible patients were identified. Baseline histories of concomitant pain and psychiatric disorders were abstracted. Ketamine infusion were started at a rate of 0.1 mg per kg and escalated as needed. Initial and follow-up on a 0 to 10 pain scale were documented as well as concomitant pain and psychiatric disorders. We defined an acute response as a reduction to a score of 3 or less.

Results: Pre-treatment pain scores for all of 6 patients were in the range 9–10. The median age was 38.8 years, and 5 out 6 patients were women. All 6 patients achieved a Pain Score of 3 or less at an average infusion rate of 8.5 mg/kg (Range:0.97–19.98 mg/kg). The median time to acute response was 32.5 hours, No typical side effects from ketamine were reported from patients.

Conclusion: Intravenous ketamine was safely administered in the hospital setting to patients with refractory chronic migraine with no significant side effects reported. Intravenous ketamine results in improvement of acute pain in severe refractory cases of chronic migraine. Future prospective and placebo-controlled trials are needed.

PO025

Migraine acute therapy

Influence of associated between migraine profilatic drugs and sumatriptan succinate over the motor activity and anxiety

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Background and aim: The clinical motor effect of Sumatriptan (S), and whether or not it is associated with various classes of prophylactic drugs for migraine has not been studied yet. This study aims to analyze the influence of such drugs in animal's psychomotor activity, verifying its effect when used either singly or in association.

Methods: W included 98 male Norvegicus rats, treated with usually prophylactic migraine drugs, divided in five groups: isotonic saline solution (ISS) (control group); propranolol (P); topiramate (T); flunarizine (F) and amitriptyline (A). After five days with daily treatment the animals received acute treatment with ISS or S. The influence of migraine prophylactic and acute treatment over the motor and anxiety behavior were assessment utilizing the rotarod and open field tests.

Results: Prophylatic drugs such as P and F interferes consistently with the motor activity ($p = 0{,}006$ and 0,002 respectively). The association S with these and other prophylactic drugs or utilized alone did not produce motor influence. Prophylactic migraine drugs did not influence the behavior of anxiety when used alone. The S when used in combination as A and F produce an anxiolytic effect. The F and S increases the latency to the onset of movements ($p = 0.031$). The A and S increases the number of withdrawals ($p = 0.045$) and reduced the immobility of animals ($p = 0.041$).

Conclusions: Our study showed no motor effect of S alone or the combination with major migraine prophylatic drugs. We showed that S when associated with A or F exhibited anxiolitic effect.

PO026

Migraine acute therapy

Benefits of AVP-825 vs. oral sumatriptan on migraine-related disability within 60 minutes: results from the compass study

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Background: AVP-825, an investigational product, provides novel Breath Powered™ Bi-Directional™ intranasal delivery of low-dose sumatriptan powder (22 mg).

Aim: Compare AVP-825 versus 100 mg oral sumatriptan tablet on headache-related disability using data from the COMPASS Study (NCT01667679), a double-dummy, active-comparator, crossover study.

Methods: Subjects were randomized 1:1 to one of two sequences of treatment: 1. AVP-825 plus placebo tablet followed by a period of identical placebo device (containing lactose powder) plus sumatriptan tablet or 2. Placebo device plus sumatriptan tablet followed by AVP-825 plus placebo tablet. Three-level ordinal multilevel

models with random effects accounted for the unique data structure (repeated measures nested within attacks for each patient) and tested for differences in rate of change in disability from pre-dose to 60 minutes (m).

Results: 259 subjects were 84.6% female, 21.6% minority, mean age of 40.0, treated a mean 6.7 attacks. Both treatments were associated with significant reductions in clinical disability from pre-dose to 10m ($p < .05$).

Conclusions: AVP-825 improved migraine-related disability more rapidly than sumatriptan tablets within the first 30 m, and had lower headache-related disability scores throughout the first hour following treatment.

PO027

Migraine acute therapy

Benefits of AVP-825 vs. Oral sumatriptan on treating migraine pain: results from the compass study

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Background: Rapid pain relief is a priority. AVP-825, an investigational product, provides novel Breath Powered™ Bi-Directional™ intranasal delivery of low-dose sumatriptan powder (22 mg).

Aim: Compare AVP-825 vs. 100 mg of oral sumatriptan on migraine pain over the first hour following treatment using data from the COMPASS Study (NCT01667679), a double-dummy, active-comparator, crossover study.

Methods: Subjects were randomized 1:1 to one of two sequences of treatment periods: 1. AVP-825 plus oral placebo tablet followed by a period of identical placebo device (containing lactose powder) plus 100 mg oral sumatriptan tablet or 2. Placebo device plus 100 mg oral sumatriptan tablet followed by AVP-825 plus oral placebo. In each period patients treated $\leq$5 qualifying migraines in $\leq$12 weeks. Three-level ordinal multilevel models accounted for unique data structure (repeated measures nested within attacks for each subject) and tested for treatment differences in the rate of change in severity from 10 to 60 minutes controlling for pre-dose pain severity.

Results: 259 subjects were 84.6% female, 21.6% minority, mean age of 40.0, and treated a mean 6.7 attacks. Subjects who treated attacks with AVP-825 experienced significantly faster rates of pain reduction at 10, 15, 30 minutes.

Conclusions: AVP-825 reduced migraine pain severity more rapidly within the first 30 minutes compared to 100 mg sumatriptan, and had lower overall migraine pain severity during the first hour of treatment.

PO028

Migraine acute therapy

20 years of triptan use in Austria

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Background: Triptans are recommended as first-line therapy in the acute phase of a migraine attack. 20 years after approval of triptans in Austria we describe patterns of triptan use in a tertiary care headache outpatient clinic.

Methods: From December 2009 until August 2012 consecutive demographic and clinical data of patients with migraine were collected. Data collection included age, gender, headache days during the month prior to consultation, prophylactic medication, triptan use, comorbidities, trigger factors, caffeine consumption and use of hormonal contraception. The Headache Impact Test (HIT-6) was used to measure the adverse impact of headaches.

Results: 511 patients were included (migraine without aura: n = 307, migraine with aura: n = 182, chronic migraine: n = 22). Upon first consultation 73.2% of all patients (n = 374) were triptan naïve. At the first follow-up visit 17.7% of all patients, who had treated their migraine attacks with a triptan between the first and the second visit, reported no or insufficient pain relief. Recurrence headache was reported by 15%. 60.5% of all patients did not refill their triptan at visit 2 or switched to a different type of triptan. Positive treatment response and low HIT-6 were associated with triptan retention.

Conclusion: The high number of patients not refilling their triptan prescription indicates that there is an unmet need in acute migraine treatment that we should understand more thoroughly in order to improve triptan retention. The HIT-6 score may be used as an indicator of triptan adherence and help to identify patients at risk for triptan discontinuation.

PO029

Migraine acute therapy

Application of ampa receptor antagonist on spatial memory after repetitive spreading depression in juvenile rats

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Background: Spreading depression (SD) is a bio-electrical wave in the central nervous system which propagates through the gray matter and cause several effects, such as neural depolarization and ionic disturbances. This phenomenon plays a role in many neurological disorders, like epilepsy, migraine with aura, brain injury and cerebrovascular disease. The SD excitatory effect of glutamate receptors on the brain seems to be correlated with neural injuries.

Aim: The aim of our study was to evaluate the role of glutamate AMPA sub receptors on spatial memory impairment induced by SD.

Materials and Methods: DNQX, an AMPA antagonist, was administrated (1 mg/kg) intraperitoneally after SD induction (induced by application of 2 M KCl; Four consecutive weeks) in juvenile Wistar rats (60–80 gr). Retrieval of spatial memory was evaluated by T-maze memory test. All the experiments were carried out according to the protocol approved by the Animal Ethics Committee of Shefa Neuroscience Center, Tehran, Iran.

Results: Repetitive weekly induction of SD caused memory impairment after four weeks. Blockade of AMPA receptors with DNQX did not affect the memory impairment caused by SD.

Conclusion: Our data indicate glutamate AMPA sub receptors are not involved in SD-induced memory deficits in juvenile rats.

Keywords: 1. Cortical Spreading, Depression, 2. Receptors, AMPA 3. Memory

PO030

Migraine acute therapy

Efficacy of bone decompression technique on migraine

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Background: Migraine has always been considered important because of the impact on the quality-of-life. Bone decompression technique by using Type T bone decompression needle are newly developed technique for treatment of Migraine.

Aim: The purpose of this study is to evaluate the therapeutic effect of Bone decompression technique for the treatment of migraine.

Method: Decompression group received Bone decompression technique by using Type T bone decompression needle once a week for 8 weeks. The drilling tip of Type T Bone Decompression Needle is 1 mm in diameter, and it penetrated into the skull bone in 5 mm. The control group received acupucture therapy once a week for 8 weeks. On the follow-up period, changes in the amount of pain were assessed by the VAS. Data obtained were analyzed using SPSS software.

Results: Variance analysis revealed a difference in the mean pain and disability score of the VAS questionnaire between two groups before and 8 week($P < 0.05$), 6 month($P < 0.05$) after the therapy. Improvement was more satisfactory in the bone decompression group.

Conclusion: The use of bone decompression technique seems to be efficacious on treatment of migraine.

PO031

Migraine acute therapy

The effectiveness of cervical facets infiltration of C2-3 in the treatment of transformed migraine (TM) plus cervicogenic component

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Objective: The objective of this study is to evaluate the effectiveness of cervical facets infiltration of C2-3 in the

treatment of transformed migraine (TM) plus cervicogenic component.

Background: Transformed migraine (TM) is a chronic, daily headache, with vascular quality. Patients usually use large doses of analgesics and experience withdrawal headaches. Cervicogenic migraine, on the other hand, is a secondary headache due to an underlying structural problem in the head or neck.

Methods: 30 patients were evaluated at the Pain & Headache Center, IMC, KSA according to IHS classification. Patients were allocated to receive either cervical infiltration of C2-3 facets on the same side of migraine (13); or oral bridge therapy (Eletriptan and Etoricoxib) which was administered daily for 15 days, and which was followed by Topiramate 100 mg daily for 6 month as a preventive therapy in both groups. Inclusive criteria: 10 males, 20 females; ages 30–50 years, with a mean of 40. Exclusive criteria: pediatrics; patients older than 50, with uncontrolled diabetes, blood pressure, other neurological deficits; or pregnancy.

Results: Average symptomatic improvement of 78%, according to numeric pain scale, was recognized in patients receiving cervical facets infiltration therapy and appreciated within 10–20 days of therapy. However, an average improvement of 58% was recognized by patients receiving oral bridge therapy and appreciated within one month of therapy.

Conclusion: Patients who received cervical facets infiltration showed more rapid and significant symptomatic improvement of their headache after the treatment as compared to the oral bridge therapy.

PO032

Migraine acute therapy

From investigational product to active reference: evolution of oral sumatriptan efficacy vs. placebo over time for the treatment of acute migraine episodes

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Background: Previous studies have shown that overall the estimated relative efficacy of widely used drugs can vary substantially over time. Possible influencers may include changes in population characteristics or variation in the placebo response. Sumatriptan was used as a treatment to examine this phenomenon as it has steadily been used as a reference treatment over time.

Aim: To assess the evolution of the relative efficacy of oral sumatriptan against placebo, between launch and the latest assessment.

Method: A systematic literature review of randomized-controlled trials (RCTs) of adults suffering from acute migraine episodes was performed in Medline. RCTs evaluating sumatriptan were included in the analyses. Efficacy outcomes evaluated included pain free (PF) and headache relief (HR) at 2 hrs and recurrence within 24 hrs. Efficacy of sumatriptan was presented as the mean difference to placebo.

Results: PF, HR and recurrence outcomes were reported in 38, 36 and 25 studies, respectively. For PF and recurrence, the relative effect of sumatriptan was found to increase over time, despite an increase in absolute placebo effect for PF. A 20% increase in the relative effect for PF was observed over time. The results need to be contrasted to the one in HR, where the relative effect of sumatriptan decreased overtime; this was partly explained by an increase in placebo effect.

Conclusion: The relative efficacy of sumatriptan on PF and recurrence vs. placebo was found to increase over time since launch. Further research is needed to understand the increase and the consequences for assessing drug relativeness effectiveness.

PO033

Migraine acute therapy

Clinical features of headache in children and adolescents at an outpatient pain clinic in Japan

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Background: Children and adolescents frequently experience headaches. Although they usually visit pediatric clinics, some of them visit pain clinics. However, there is little information about the clinical features and therapeutic efficacy of headache patients who visit pain clinics.

Objective: To investigate the clinical features of children and adolescents who visit an outpatient pain clinic for management of headaches as well as the efficacy of the treatments.

Methods: In this single hospital-based retrospective study, we enrolled patients aged ≤15 years, who had headache and visited our pain clinic between 2013 and 2014. We obtained information on clinical background, diagnosis, response rate and adverse effects of acute-phase therapy, and prognosis from their medical records.

Results: Twenty-two patients (M:F = 8:14; age, 12.1 ± 2.6 years) were enrolled. Twenty of the 22 patients (91%) were diagnosed as having migraine, including migraine without aura (13 patients; 59%), migraine with aura (7 patients; 32%), and secondary headache disorders (2 patients; 9%). Eighteen of the 22 patients (82%) had already received medical treatments at previous hospitals, although headache was not treated successfully. Acetaminophen was not effective for these patients. However, triptans such as rizatriptan and eletriptan were used for the treatment of the headache in 14 of 20 patients with migraine, and all patients were treated successfully. Triptans did not produce serious adverse effects. Patients did not prefer nasal sumatriptan because of its bitter taste.

Conclusions: More than 90% of children and adolescent patients with headache who visited a pain clinic had migraine. Triptans were effective and well tolerated.

PO034

Migraine acute therapy

Experiences of an outpatient infusion program of an academic headache center with intravenous magnesium therapy

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Background: Oral magnesium has been used extensively as preventative treatment for migraine headache, but there is only limited information on its intravenous use as an acute abortive agent for headaches in an outpatient setting.

Aim: To determine the feasibility and effectiveness of intravenous magnesium in an infusion center.

Method: Cross-sectional study of 88 patients treated at an academic center with a diagnosis of chronic migraine with status migrainosus, except 1 who had chronic cluster headaches. Intravenous magnesium sulfate (2 g diluted with 50–100 cc of normal saline) was administered over 1–2 hours. Immediately before and after infusion, pain levels were recorded using the Wong-Baker FACES Pain Rating Scale (0–10. Additional intramuscular (IM) injections for nausea (prochlorperazine) or for refractory pain (ketorolac and dexamethasone), were administered as necessary.

Results: The majority of patients were female (n = 69) with mean age 48 ± 17. 32 patients received intravenous magnesium only, and 56 received additional IM injections after the infusion; 39 received ketorolac, 30 received dexamethasone, and 28 received prochlorperazine. There was a significant reduction in pretreatment pain score 5.47 ± 2.91 to 3.33 ± 2.62 ($P < 0.001$) after intravenous therapy. In patients who received intravenous magnesium only, pain score decreased from 4.78 ± 3.18 to 2.84 ± 2.37 ($p < 0.001$). In patients who received additional IM injections, pain score decreased significantly from 5.69 ± 2.78 to 3.61 ± 2.74 ($p < 0.001$).

Conclusion: Intravenous magnesium, with or without intramuscular medications can result in significant relief in pain of status migrainosus. Outpatient infusion centers can be efficient and cost-effective way to providing headache rescue treatment, decreasing the need for emergency room visits.

PO035

Migraine preventive therapy

Eyelid myokymia in patients with migraine taking topiramate

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Background: Although ocular side effects of topiramate arecommon, neuroophthalmologic manifestations such as blepharospasm, myokymia andoculogyric crisis are scarcely reported. We present a series of 8 patients withmigraine who developed eyelid myokymia after treatment with topiramate.

Methods: We reviewed all patients with migraine treated with topiramate attending theheadache outpatient clinic of our hospital from January 2008 to December 2012. During the study period, a total of 140patients

with migraine were treated with topiramate in our headache clinic.

Results: Eight presentedeyelid myokymia after beginning treatment with topiramate (5,7%). Topiramate was stopped and myokymia disappeared inall patients, it was prescribed again and eyelid myokymia reappeared with theirprevious characteristics in all patients.

Conclusion: Eyelid myokymia is an underreported side-effect oftopiramate in patients with migraine, of unknown cause, so that futures furtherstudies need to examine whether patients with migraine are predisposed or notto this adverse effect.

Keywords: migraine, topiramate, neuroophthalmologic manifestations ocularside effects, myokymia, eyelid myokymia.

PO036

Migraine preventive therapy

Comparing the effect of wet-cupping and temperament reform on the severity of migraine headaches

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Aims: Migraine is a chronic and invasive neurological disorder which is recognized by severe episodic and recurrent headaches. Nowadays use of non-pharmacological methods to relief pain are in progress. This study was done to compare the effect of wet-cupping and temperament modification on pain intensity in patients with migraine headache.

Methods: This clinical trial was done in patients with migraine referring to Quchan traditional medicine official Center in 2012. 198 patients were selected by convenience sampling method and were studied. To collect data, two-part questionnaire (demographic characteristics and characteristics of headache) and a pain intensity form based on the visual analogue scale were used. After homogenizing the samples, they were randomly divided into three wet-cupping, temperament modification and control groups. Paired T, Kruskal-Wallis and Mann-Whitney tests were used to analyze the data.

Results: The mean of pain intensity in the three groups of temperament modification (7.5 ± 1.2), wet-cupping (7.6 ± 1.3) and control (7.2 ± 1.2) before intervention showed no significant difference ($p = 0.401$). There were a significant difference between the mean of pain intensity of temperament modification (6.6 ± 1.2), wet-cupping (2.4 ± 1.9) and control (0.6 ± 0.8) groups before and after interventions ($p < 0.001$).

Conclusion: Wet-cupping and temperament modification are very effective tools to treat migraine headaches.

PO037

Migraine preventive therapy

Effect of transcranial magnetic stimulation on cellular anatomy after repetitive cortical spreading depression

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Background: Spreading depression (SD) is a phenomenon where homeostatic electrochemical properties of many cell types in the brain are altered, often accompanied by morphological changes in neuronal cells. This is often the result of propagating chronic cell depolarization. Previous study proved correlation of many neurotransmitter releases such as Glutamate and GABA with this phenomenon. Hippocampus is the most vulnerable area for SD and most of cell death is observed in this region. Various drugs have been tested for Migraineurs working through different mechanisms.

Aim: Recent study has stood to reason that maybe changing in brain electrical activity could inhibit SD wave initiation. Present study tested transcranial magnetic stimulation (TMS) in rats. Method: The number of 94 Wistar rat were subjected in four groups including controls, SD, TMS treatment, and TMS control. TMS have been administrated four a month daily and SD was induced by induction of KCl

Through cannula over somatosensory cortex for four continues weeks and behavioral test was performed and the rats were perfused transcardially for histological studies.

Results: Data from shuttle box test show no significant improvement in treated rats compare to SD animals. However, histological analyses have revealed significant changes in some region of hippocampus including dentate gyrus and CA1.

Conclusion: Our result showed that SD have a complicated pathophysiology and changing in electrical activity and increasing inhibitory neurotransmitter by TMS could not significantly inhibit SD initiation as well as memory impairment induced by SD or protect neural damage in hippocampus areas.

PO038

Migraine preventive therapy

Increased rate of venous thrombosis associated with inpatient dihydroergotamine treatment

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Background/Aim: Repetitive dosing of intravenous dihydroergotamine (DHE) is used for inpatient treatment of chronic migraine. Since DHE is a venoconstrictor, maintaining vascular access during a longer course can be difficult and thus peripherally-inserted central (PICC) or midline catheters are often employed. We noted a number of venous thromboses and sought to review whether the incidence was higher than would be expected.

Methods: We reviewed all admissions at the UCSF Headache Center from February 25, 2008 through October 31, 2014 for the following variables: age, sex, diagnosis, presence of aura, relevant medical history, treatment and dose, type of intravenous line used, days with line, superficial or deep venous thrombosis, and pulmonary embolism.

Results: PICC or midline catheter was placed in 318 of 604 admissions (213 patients). These patients were ages 7 to 79 (mean 36.3 years; 74 patients age 18 or under), 82% female, and 24% had aura. DHE was given to 265 and lidocaine to 53. Nineteen thrombotic events (7.2%) in 19 patients occurred with DHE treatment: 18 PICC or midline-associated thromboses (deep 10, superficial 6, pulmonary embolism 2) and one saphenous vein thrombosis. No thrombotic events occurred with lidocaine treatment. Age, sex, presence of aura, line type, days with line, and DHE dose were not significant predictors, although days with line showed a trend toward significance.

Conclusions: Intravenous dihydroergotamine treatment may be associated with an increased risk of venous thrombosis. A low threshold for ultrasound investigation and consideration of prophylactic anticoagulation are appropriate.

PO039

Migraine preventive therapy

Short-term effects of greater occipital nerve blockades in chronic migraine: a double-blind, randomized, placebo-controlled clinical trial

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Background: Greater occipital nerve (GON) blockades are widely used for the treatment of headaches. Yet, its efficacy in migraine has hardly been assessed with controlled studies.

Aim: To assess the short-term clinical efficacy of GON anaesthetic blockades in chronic migraine and to analyze their effect on pressure pain thresholds (PPTs) in different territories.

Methods: This study was designed as a double-blind, randomized and placebo-controlled clinical trial. Twenty-six women with chronic migraine were treated either with bilateral GON blockade with bupivacaine 0.5% ($n = 13$) or placebo ($n = 13$). Headache days were recorded during the week before and the week after the procedure. PPTs were measured in cephalic points (supraorbital, infraorbital and mental nerves) and extra-cephalic points (hand, leg) just before the injection, 1 hour later and 1 week later.

Results: Treatment with anaesthesia was superior to placebo in the reduction of the number of days per week with moderate or severe headache (MANOVA; $p = 0.003$), or any headache ($p = 0.005$). In addition, patients treated with anaesthesia showed PPT increases at the cephalic points, which were significant compared to placebo ($p < 0.05$) except for the left supraorbital nerve. PPT changes did not differ significantly between groups at the extra-cephalic points.

Conclusions: GON anaesthetic blockades seem to have short-term efficacy in chronic migraine, as measured by a reduction in the number of days with moderate-to-severe headache or any headache during the week following injection. GON blockade is followed by an increase in PPTs at the trigeminal area, suggesting an effect on central sensitization at the trigeminal nucleus caudalis.

PO040

Migraine preventive therapy

The acumigran study: a randomized controlled clinical trial on the efficacy of acupuncture for migraine prophylaxis

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Background: the efficacy of acupuncture for migraine prophylaxis still remains controversy.

Aim: to evaluate the efficacy of acupuncture compared to that of pharmacological treatment as prophylaxis for migraine with and without aura.

Method: this is a randomized controlled clinical study. Patient suffering from migraine without preventive treatment in the past three months were recruited. After the run-in period episodic migraineurs were assigned randomly to two groups: the acupuncture group (A) was treated with 12 sessions of acupuncture and the pharmacological group (B) was treated with the most appropriate medication for each patient. Headache frequency was compared at baseline and at the end of treatment.

Results: A total of 85 patients (15 males and 70 females) were enrolled in this study. Out of these, 42 were randomized at A and 43 at B. At baseline no significantly differences were found between the two groups. Of the overall sample 56 patients completed the protocol. After 4 months, the migraine frequency decreased from 9.26 ± 3.17 to 6.00 ± 3.58 in A and from 7.95 ± 2.78 to 6.24 ± 3.90 in B. Headache frequency decreased significantly after treatment without differences between the two groups (time-effect: $p < 0.001$; group effect: $p = 0.709$; interaction time-group effects: $p = 0.437$). Responders (migraineurs with a reduction of headache days by at least 50%) were 44.12% in A and 38.10% in B ($p = 0.660$).

Conclusion: our preliminary data suggest that acupuncture was as effective as pharmacological treatment in decreasing migraine frequency.

This study was funded by II Programma sperimentale regionale per l'integrazione delle MNC nel servizio sanitario dell'Emilia-Romagna.

PO041

Migraine preventive therapy

Therapeutic effect of memantine as a preventative treatment for migraine: a prospective, open-label clinical trial

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Objective: Assessing the efficacy of memantine as a preventative migraine treatment and its potential side effects.

Background: Prophylactic migraine treatment has always been a challenge. Efficacy and tolerability are two main issues in current approved migraine prevention. Since some migraine patients fail approved preventative agents, experts are always seeking newer agents. Memantine, a glutaminergic antagonist, could potentially be one of these agents.

Design & Methods: 127 migraine patients meeting the criteria for starting preventative therapy (>4 headache days/month) are included in the study. All patients previously failed at least one trial of adequate preventive therapy. After a 30 day baseline observation, patients started memantine for 3 months, beginning at 5 mg/day, which increased by 5 mg/week up to a maximum of 20 mg a day if symptoms did not improve. Headache frequency, duration, and severity were assessed at the end of the treatment phase. 102 patients completed the study.

Results: In the study population, headache frequency reduced from 9.9 days/month at baseline to 5 days/month at 3 months ($P < .001$). The mean severe pain reduced from 6.9 to 3.6 at 3 months ($P < .001$). Headache duration significantly reduced at 3 months, compared with baseline ($P < .001$).

Side effects related to memantine consumption were uncommon and generally mild.

Conclusion: Based on preliminary data, there is some evidence that memantine might be useful in the treatment of refractory migraine. This is in line with previous pilot and open label studies. However, double blind studies are still needed.

PO042

Migraine preventive therapy

Long term outcome of patients with chronic migraine treated with onabotulinumtoxina. A prospective two year follow up of 170 patients treated in hull, UK

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Background: OnabotulinumtoxinA is licensed for treating adult patients with Chronic Migraine (CM). The National Institute for Clinical Excellence (NICE) in the UK approve its use on the NHS provided patients have failed three preventive treatments and medication overuse is addressed. Treatment is discontinued with lack of response at cycle 2 (negative stopping rule) and when the migraine become episodic (positive stopping rule). However the long term outcome i.e., duration of treatment, sustained benefit after stopping treatment and the rate of relapse after stoppage remains unclear.

Aim: To determine the long term outcome of patients treated with OnabotulinumtoxinA in the prevention of CM.

Methods: All patients receiving OnabotulinumtoxinA for CM at the Hull Migraine Clinic were followed up and data for headache, migraine and headache free days were extracted from headache diary. Responders were defined as per NICE criteria with 30% reduction on headache days at cycle 2. Negative stopping rule was applied as per NICE recommendation, although responders were offered treatment until the headache days were reduced to <10 for three consecutive months.

Results: 170 responders at cycle 2, only 70 patients had successfully stopped treatment and showed a sustained benfit; 10 became resistant to treatment after initial response. 90 patients were still on treatment at two years of which 45 relapsed having previously stopped treatment.

Conclusion: Only 40% of patients show sustained benefit after stoppage while 53% remain on treatment at two years. 6% become resistant after initial benefit and 50% of patients relapse after stopping treatment.

PO043

Migraine preventive therapy

Flunarizine in primary headache disorders

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Background: Flunarizine is a widely used migraine preventive not licensed in the UK. In September 2014, the National Institute for Clinical Excellence (NICE) published supportive guidelines for flunarizine use in migraine based on available randomised controlled evidence.

Aim: To collect data for an audit of flunarizine use from our tertiary headache practice in the UK over twenty years, to try to establish indications for its use, typical doses, short and long term side effects, and treatment outcomes, including changes in acute treatment use and change in frequency and intensity of headache on treatment.

Results: For the first 30 patients audited the most common indication for flunarizine was chronic migraine, followed by migraine with aura, sporadic hemiplegic migraine and familial hemiplegic migraine and then new persistent daily headache of a migrainous type. Doses up to 15 mg were generally well tolerated, with only five patients stopping treatment due to adverse effects. Flunarizine is generally effective; with only three patients reporting no clinical effect: two had hemiplegic migraine and one chronic migraine. The commonest dose used was 10 mg and a significant proportion of patients continued treatment for more than one year.

Conclusion: Flunarizine is an effective, well tolerated migraine preventive that can be used for extended periods in a range of migraine sub-types.

PO044

Migraine preventive therapy

Are blue-light blocking eyeglasses beneficial to migraine patients?

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Background: Intrinsically photosensitive retinal ganglion cell (ipRGC) are reportedlylinked to the photophobia of migraine headache. We have demonstrated thatmigraine patients find blue light to be bright. Recently, blue-light blockingeyeglasses have come into widespread use in Japan, though their benefits inmigraine patients remain uncertain.

Aim: This study aimed to investigate whetherthe use of blue-light blocking eyeglasses reduces headache attacks in migrainepatients.

Method: Six migraine patients served as studysubjects. We prepared three types of eyeglasses with different rates of lighttransmission. The subjects wore each type of eyeglasses for one month duringtheir daytime working hours. Lens A moderately blocks short-wavelength light-only. Lens B provides a high degree of blockage of short-wavelength light only. Lens C blocks short- and long-wavelengths of light equally. The subjects alsospent one month not wearing any eyeglasses. The following data were analyzed foreach subject: the number of days with headache and medication days, score on the HIT-6.

Results: In the six migraine patients, the mean number of days withheadache was 7 with lens A, 7 with lens B, 5.7 with lens C, and 5.8 with noeyeglasses. The mean number of medication days was 4.2 with lens A, 4.8 withlens B, 3.7 with lens C, and 3.8 with no eyeglasses. Compared to no eyeglasses, lenses A, B and C did not demonstrate significant improvement in the mean HIT-6.

Conclusion: Daytime use of blue-light blocking eyeglasses does not appear to reduceheadache attacks in migraine patients.

PO045

Migraine preventive therapy

A proposal for safe and efficient botulinum toxin injection points of frontal area in chronic migraine

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Botulinum toxin type A (BoNT-A) has been reported as an effective treatment for chronic migraine. When BoNT-A is injected on the frontalis muscle for chronic migraine, an unexpected clinical side effect called the "Mephisto sign" may occur. The aim of this article is to propose botulinum toxin injection points of frontal area to eliminate or prevent the Mephisto sign side effect.

A 25-year-old female patient visited the hospital and was diagnosed with chronic migraine. A total of 155 U of BoNT-A was injected into 31 sites. 2 weeks later, and the patient developed the Mephisto sign. An additional 2-U dose was administered bilaterally to the lateral-most point of the frontalis muscles, and the eyebrow morphology returned to normal within 2–3 weeks.

We propose that the development of the Mephisto sign may be prevented with an additional BoNT-A injection of 2–4 U bilaterally to the lateral most point of the frontalis muscles during the primary injection process.

PO046

Migraine preventive therapy

Prospective analysis of the use of onabotulinumtoxina (Botox) in the treatment of chronic migraine; real-life data in 419 patients from hull, U.K.: an update!

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Background

- Chronic migraine (CM) affects 2% of the general population with substantial impact on quality of life.
- The efficacy and safety of Botox in CM was confirmed in the phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical programme. Despite this, few data exist in the real-life setting

Aim
- To evaluate the efficacy of Botox in adults with CM in real-life setting

Method
- Adult patients with CM attending the Hull migraine clinic were offered Botox based on clinical needs using the PREEMPT protocol
- Headache diaries were maintained for at least 30 days prior to and continuously after Botox (July 2010 and December 2014)
- Data were extracted for headache, migraine, and headache-free days
- A responder was defined as one with **either**
  - oa 50% reduction in either
  - headache days
  - or migraine days
  - oan increment in crystal clear days twice that of the baseline

Results
- Of a series of 507 patients, full data were available on 419 patients
- There was significant decrement in headache and migraine days as well as similarly significant increment in headache-free days
- Responder rate was calculated for the above mentioned 3 categories

Discussion
- Our cohort represent a more severely affected population than seen in PREEMPT study; furthermore the pre-treatment headache days' number was higher in our patients

Conclusion
- Our analysis has shown that, in a real-life clinical setting, Botox can effectively reduce headache and migraine days, and increase crystal clear days from baseline.

PO047

Migraine preventive therapy

The migraine prophylactic effect of candesartan and telmisartan on rat CSD model

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Background: It is speculated that obese person's hyperleptinemia have some kinds of association with migraine. Leptin chronically elevates the sympathetic nervous system and activates the renin–angiotensin system.

Aim: In this time, we examined the migraine prophylactic effect of first generation ARB (Candesartan) and second generation ARB (Telmisartan which has effect of PPARγ agonist) on rat CSD model.

Methods: Fifty male Sprague Dawley rats were used. Migraine prophylactic drugs (candesartan 16 mg/kg, telmisartan 1 mg/kg) or saline (as vehicle) was administered orally once a day for 28 days (respectively $n = 5$). Under anesthetizing condition, tracheostomy was performed for controlled ventilation. The three bone fenestrations were opened for measuring cerebral blood flow (CBF), direct current (DC) potential and for dropping KCl solution. 1.0 M KCl solution was applied through the bone fenestration onto the cortical surface to induce CSD.

Results: There was no significant difference with between candesartan and vehicle in % change of CBF, % change of DC potential, the number of CSDs and the duration of CSD. The number of CSDs and the duration of CSD were significantly decreased by telmisartan compared with vehicle.

Conclusions: Inflammatory cytokines (e.g. tumor necrosis factor-α (TNF-α)) and CGRP which have some relationship with pathogenesis of migraine are increased by leptin. It is reported that PPARγ agonistic activity of telmisartan is stronger than that of candesartan. PPARγ agonist which has anti-inflammatory effects increased adiponectin and decreased TNF-α. Migraine prophylactic effect of telmisartan may depend on its PPARγ agonistic activity. Telmisartan may have stronger migraine prophylactic effect compared with candesartan.

PO048

Migraine preventive therapy

Study of low dose topiramate in migraine prevention in southern indian rural population

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Objective: This study was conducted to assess the efficacy of Low dose topiramate to prevent the frequency of migraine headache in young rural Indian Patients.

Method: This Prospective Study was Conducted in patients who met IHS criteria for migraine for the period of one year from 1st January 2014 at ABC hospital Trichy Tamilnadu India. In all patients Migraine headache

frequency were recorded and it response to low dose of 50 mg topiramate along with the incidence of side effects were recorded and analyzed.

Results: Frothy two patients [Male 16 Female 26] were studied. The age of the patients ranges from 16 to 40 with the mean age of 26 years. The mean duration of headache was 12 years. The mean duration of topiramate therapy was 33 weeks. All the patients received topiramate monotherapy. Folic acid was prescribed to female patients in reproductive age group. Thirty patients [71.42%] were experienced more than 71% reduction in the migraine headache frequency.

The common of Side effect was drowsiness in 12, tingling Sensation in 2, dysmenorrheal in 3 and purities in one. One patient discontinued the treatment due to itching. Dose reduction to 25 mg was made in 10 patients to with drowsiness.

Conclusion: In this study low dose topiramate shows reduction in migraine headache frequency more than 70% of young rural Indian patient. To primate is well tolerated in low dose in India rural patient with any problem with their daily day today activities.

PO049

Migraine preventive therapy

Botox in chronic migraine prevention: predicting response to treatment based on headache days at baseline

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Background

- Chronic migraine (CM) affects 2% of the general population with substantial impact on quality of life.
- Botox is licensed for CM prevention and 50–70% patients improve with reduction of headache/migraine days.
- However, predictors of response to treatment are unknown.

Aim

- To establish whether the number of headache days at baseline could predict response to treatment with Botox in patients with CM.

Method

- Data was collected from all patients attending the Hull Migraine Clinic between July 2010 to December 2014 using a dedicated headache diary.
- Patients were categorised into three groups based on headache frequency at baseline; low (16–20 days), medium (21–25 days) and high (26–30 days).
- Responders were defined as per NICE criteria (30% reduction in headache days) and Hull Criteria (50% reduction in either headache or migraine days or increase in headache free days twice that of baseline (provided there were at least 3 headache free days before treatment)

Results

- Of a series of 507 patients, full data were available on 419 patients.
- Using NICE criteria 54.8% (N = 82) of low frequency and 54.7% (N = 95) of medium frequency showed response compared to only 33.8% (N = 242) of high frequency sufferers.
- Applying Hull Criteria 73.6% (N = 95) of medium frequency showed response compared to 59.1% (N = 242) and 51.2% (N = 82) of high and low frequency respectively,

Conclusion

- Our analysis suggests patients with 16–25 days of headache at baseline seem to respond better to treatment with Botox.
- There may be other compounding factors to explain this finding which is being looked at.

PO050

Migraine preventive therapy

Predictor factors influencing the response to botulinum toxin type a (BoNTA) in chronic migraine: a new therapeutic strategy

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Background: Some patients with chronic migraine (CM) are unresponsive to treatment with botulinum toxin type A (BoNTA) through PREEMPT paradigm. Whether there are factors influencing the response to BoNTA treatment in patients with CM is poorly understood.

Aim: To evaluate whether cutaneous allodynia (CA), location and methods of injection influence the efficacy of BoNTA treatment.

Method: sixty four consecutive patients with CM unresponsive to BoNTA treatment were evaluated for detecting both the location of the pain and the severity of CA, then they underwent either trigeminal or occipital/cervical subcutaneous/intramuscular injections of BoNTA. During the follow up patients were evaluated at 30 and 60 days. Primary end-point was change >50% in number of monthly headache-free days. Moreover, the same patients were treated with false injections in the area of verum treatment.

Results: According to location of the pain and severity of CA, patients were categorized in 2 groups: Group 1, allodynic patients with trigeminal location of pain, performed subcutaneous BoNTA injections in the trigeminal area; Group 2, non-allodynic patients with occipital location of pain, performed subcutaneous/intramuscular injections in occipital/cervical area. The treatments decreased significantly the number of monthly headache-free days in 56% of patients in Group 1, and 43% of patients in Group 2. The efficacy lasted about 60 days. While, few patients had a temporary response to false treatment.

Conclusion: The severity of CA, the location and the methods of injection are factors influencing the efficacy of BoNTA in unresponsive patients with CM.

PO051

Migraine preventive therapy

Interim analysis of the real-world utilization and safety of onabotulinumtoxina for the prophylactic treatment of chronic migraine in an observational study in the European Union

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Background: OnabotulinumtoxinA is approved for chronic migraine (CM) headache prophylaxis with safety/efficacy established in several controlled trials. However, it is important to evaluate utilization and safety in a real-world setting.

Aim: Describe the safety and utilization of onabotulinumtoxinA for CM in routine practice.

Methods: This is a prospective, observational, multinational, European post-authorization study (NCT01432379). Data are collected at the first study injection and approximately every 3 months for ≤52 weeks (utilization) or ≤64 weeks (safety). Data as of March 10, 2014 are summarized using descriptive statistics.

Results: Physicians at 58 sites across UK, Germany, Spain, and Sweden collected data from 1160 patients. Average patient age was 47 years (SD = 12); 84% female. To date, 162 patients (14%) completed the study and 2940 onabotulinumtoxinA treatments were administered across up to 6 treatment sessions per patient. In treatment session 1 (n = 1160), the number of injections (mean = 31) and specific muscle areas injected were similar between countries; majority of patients (78%) received 150–200 total dose units. 227 patients (20%) reported ≥1 treatment-related AE (TRAE) resulting in 33 (3%) discontinuations; 1 TRAE was serious (worsening migraine). Most commonly reported TRAEs: neck pain (3%) and eyelid ptosis (3%). Three patients (0.3%) reported treatment-related dysphagia.

Conclusions: Safety/tolerability data are consistent with previously published findings, which is in line with the known safety profile of onabotulinumtoxinA for CM. No unexpected TRAEs were reported. OnabotulinumtoxinA utilization during treatment session 1 appears to be consistent with aspects of the published PREEMPT injection paradigm.

PO052

Migraine preventive therapy

The impact of regular lifestyle behaviour in migraine: a prevalence case-referent study from a quaternary headache clinical centre

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Background: Regular Lifestyle Behaviour (RLB) of sleep, exercise, mealtime and hydration pattern independently affect migraine occurrence.

Aim: We evaluate the statistical differences of migraine occurrence among participants who do and do *not* maintain RLB.

Method: Cases of Chronic Migraine (CM) and referents of Episodic Migraine (EM) were continuously enrolled from a retrospective chart review between January 1st – June 1st, 2014 at the Stanford Headache and Facial Pain Program. Inclusion criteria were patients 15 years and older, and charts documenting RLB notes. Exclusion criteria were age younger than 15 years of age, and charts not documenting notes on RLB. Connection between prevalence of RLB and migraine attacks was measured using crude Odds Ratio (OR), Relative Risk (RR), Absolute Risk Reduction (ARR), RR Reduction (RRR), and Numbers Needed to Treat (NNT).

Results: Fifty CM cases and 50 EM referents (median age 50, 43 years; 16%, 20% males, respectively) were enrolled. Diagnosis of migraine was made according to ICHD-3 beta version criteria, and every diagnosis was confirmed by a Headache Specialist attending the Referral Clinic. The CM group (12%) exhibited less RLB than the EM group (66%, Figure 1); crude OR of 0.07 (95% CI 0.025, 0.197; $p = 0.0001$). The RLB+ (patients *with* RLB) cohort (15.4%) exhibited less CM than the RLB− (patients *without* RLB) cohort (72.1%); crude RR of 0.213 (95% CI 0.100, 0.453; $p = 0.0001$) with ARR, RRR, NNT of 56.7%, 78.6%, 1.76, respectively.

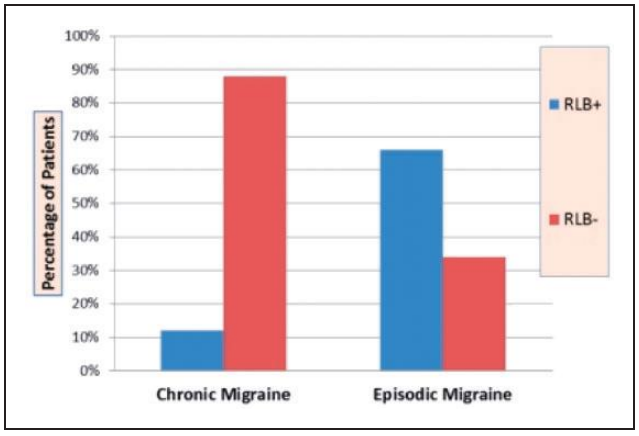

Figure 1. Difference in prevalence of regular lifestyle behaviour (RLB) among the chronic and episodic migraine cohorts. There was lower prevalence of patients having RLB (RLB+) among the chronic migraine (CM) cohort (12%) (*blue bar* on chronic migraine) compared to the episodic migraine (EM) cohort (66%) (*blue bar* on episodic migraine). There was higher number of patients *without* RLB (RLB−) among the CM cohort (88%, *red bar on* chronic migraine) compared to the EM (34%, *red bar on* episodic migraine) cohort.

Conclusion: Engaging in Regular Lifestyle Behaviour (RLB) is protective against developing Chronic Migraine.

PO053

Migraine preventive therapy

A new digital platform (curelator headache™) to identify possible migraine triggers and warning signs in individuals and test triggers for causality

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Migraine attacks may be triggered by combinations of internal (e.g. hormonal) and external (diet, environment, lifestyle) factors which differ markedly between individuals. Successful identification of triggers in individuals requires daily entry of data about lifestyle: statistical analysis of trigger-attack associations requires information about when a trigger IS and IS NOT followed by an attack. We have developed a proprietary digital platform to collect daily data, identify trigger-attack associations and propose 'tests' of trigger modifications. By increasing an individual's knowledge about their triggers and enabling them to improve their condition by modifying these, they are empowered to manage their lifestyle, improve quality of life and reduce healthcare utilisation. To obtain the required high quality daily data, Curelator Headache includes a quick, easy to use, individually-customised user interface which aims to give a high degree of compliance with, and adherence to, many weeks of data entry. To test this, over 500 people with migraine have been recruited on-line to use Curelator Headache for (initially) 90 days. Compliance and adherence are being assessed, as is the ability to generate personal Trigger Maps™ (a prerequisite for causality testing), using algorithms previously described (2). Results of this testing will be presented.

(1) Spierings ELH et al. Curr Pain Headache Rep (2014) 18:455. (2) Peris F et al. (2015) in preparation.

PO054

Migraine preventive therapy

Flunarizine for treatment of chronic migraine: subgroup analysis of patients with/without medication overuse

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Background: Patients with chronic migraine and medication overuse (CM+) are difficult to treat, and have a greater tendency towards a poorer quality of life than those with other types of headache.

Aim: The aim of this study was evaluate whether the presence of medication overuse lowers the effectiveness of flunarizine.

Patients and methods: A series of patients with CM were grouped according to whether they met medication overuse criteria or not.

Treatment with flunarizine was established from the beginning. The number of days with migraine and headache, the previous month and at four months of treatment was evaluated.

Results: In all, 259 patients with CM criteria and ITT were selected and 215 (83.0%) of them fulfilled overuse criteria. In both groups there was a significant reduction in the number of days with migraine and headache/month at the fourth month of treatment with flunarizine. (CM−), 21.8 to 8.0 and (CM+) 23.2 to 8.6, with not differences between groups.

The mean percentual reduction in the number of days with headache/month in CM without abuse (CM−) was 61.9 %, and CM+, 63.3 % (*p*.8321) and response rate (>50%) was (CM−) 75% and (CM+) 74%.

Treatment discontinuation: (CM−) was 9.0%, and (CM+) 10.2%, (p.8163).

Conclusions: Flunarizine was effective in patients with (CM−) and (CM+) and your effectiveness was similar in both subgroups.

PO055

Migraine preventive therapy

The presence of medication overuse in patients with chronic migraine affects the effectiveness of topiramate

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Background: Patients with chronic migraine and medication overuse (CM+) are difficult to treat, and have a poorer quality of life than those with other types of headache.

Aim: The aim of this study was evaluate whether the presence of medication overuse lowers the effectiveness of topiramate.

Patients and methods: A series of patients with CM were grouped according to whether they met medication overuse criteria or not.

Treatment with topiramate was established from the beginning. The number of days with headache the previous month and at four months of treatment was evaluated.

Results: In all, 264 patients with CM criteria and intention-to-treat analysis (ITT) were selected and 168 (63.6%) of them fulfilled overuse criteria. In both groups there was a significant reduction in the number of days with headache/month at the fourth month of treatment with topiramate.

The mean of reduction in the number of headache/month in CM without abuse (CM−) was 58.1%, and CM+, 48.5 % (*p* 0.0634) and response rate (>50%) was 69.5% (CM−) and (CM+),56.5%.

Treatment discontinuation: (CM−) was 20.8%, and (CM+) 26.3%, (p 0.3713).

The secondary analysis assessed 199 patients who received all treatment and completed the study. The mean of reduction in the number of days with headache/month in (CM−) was 72.1 %, and CM+, 61.8 % ($p = 0.0370$).

Response rate (>50%) according to the number of headache/month in (CM−) was 91%, and (CM+), 72%.

Conclusions: Topiramate was effective in patients with (CM −) and (CM+), although effectiveness was lower in (CM+).

PO056

Migraine preventive therapy

Suboccipital injection for migraine prevention

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Background: Migraine is a primary headache disorder for which suboccipital injections have been used for prophylaxis. These injections are given to block the greater occipital nerve which terminates at C2 spinal segment adjacent to the trigeminal nucleus caudalis. Altering the greater occipital nerve afferents modulates the trigeminal pain pathways.

Aim: To find the efficacy and tolerability of suboccipital injection in the prevention of migraine.

Method: This was a prospective interventional study of 12 migraine patients. Ethical committee approval was obtained. Informed consent was obtained from the participating patients. 3 ml lignocaine and 2 ml (80 mg)methylprednisolone(suspension) injection were used for blocking the greater occipital nerve.A 50% or greater reduction in headache frequency (as assessed by headache diary) was deemed as a positive outcome. A seven point likert scale was used as a secondary outcome variable. Patients aged 18–75 years who satisfied ICHD-2 criteria for migraine were included. Patients who were pregnant or lactating and for whom prophylactic drugs were started within the past two months were excluded.

Result: Out of 12 patients 2 did not develop scalp anesthesia following block and so were excluded. Out of the remaining 10 patients 50% of patients had a positive outcome (>50% reduction of pain). The likert scale shows that there was no negative response. 60% of the patients had a good outcome on likert scale. There were no significant side effects from the procedure.

Conclusion: This study shows that suboccipital injection has good efficacy in migraine prevention and is a relatively safe procedure.

PO057

Migraine preventive therapy

Onabotulinumtoxina in chronic migraine

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Background: Chronic migraine (CM) reduces quality of life and increases disability. OnabotulinumtoxinA is indicated for CM prophylaxis in adults with CM.

Aim: The aim of this study was to assess the effectiveness of onabotulinumtoxinA on Migraine Disability Assessment (MIDAS) questionnaire scores and a number of analgesic use in CM patients.

Method: We retrospectively evaluated CM patients who received onabotulinumtoxinA injections in our Neurology outpatient clinic between April 2012 and December 2014. MIDAS, MIDAS A, MIDAS B scores and the number of analgesic use were taken prior to the first injection (MIDAS1, $n = 85$) and every 12 weeks following the first injection (MIDAS 2, $n = 48$), (MIDAS 3, $n = 32$) and (MIDAS 4, $n = 19$). OnabotulinumtoxinA injections were repeated for three cycles.

Results: A total of 85 patients (88% female, mean age $38.70 \pm 9{,}72$) were statistically evaluated. OnabotulinumtoxinA treatment statistically significantly reduced MIDAS, MIDAS A, MIDAS B scores and the number of analgesic use between the first, second and third visit compared to baseline (MIDAS1). Comparison of MIDAS scores was (MIDAS2 ($18{,}97 \pm 20{,}57$) /MIDAS 1 ($57{,}08 \pm 20{,}90$) ($p \leq 0.01$), (MIDAS3 ($14{,}40 \pm 15{,}33$) / MIDAS 1 ($57{,}08 \pm 20{,}90$) ($p \leq 0.01$), (MIDAS4 ($7{,}36 \pm 6{,}39$) /MIDAS 1 ($57{,}08 \pm 20{,}90$) ($p \leq 0.01$). Statistically significant reductions were also observed of the number of analgesic use between the second ($8{,}17 \pm 7{,}09$) ($p \leq 0.01$), third ($9{,}19 \pm 9{,}76$) ($p \leq 0.01$), fourth visit ($3{,}20 \pm 2{,}30$) ($p \leq 0.001$) compared to baseline ($25{,}37 \pm 27{,}29$).

Conclusion: Repeated treatment with onabotulinumtoxinA was not only efficient on reducing all MIDAS scores and the number of analgesic use compare to baseline in CM patients but also safe and well tolerated.

PO058

Migraine preventive therapy

The anti-inflammatory effect of aerobic exercise correlates with clinical and mood improvement in women with episodic migraine. A randomized, controlled trial

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Background: Pro-inflammatory cytokines have been linked to several pain and mood disorders, including migraine (M). Moderate aerobic exercise training (AET) is believed to promote anti-inflammatory effects and it has been shown effective for M prevention.

Aims: We intended to explore the effect of AET on clinical outcomes, anti- and pro-inflammatory cytokines, and mood in M patients.

Methods: We conducted a RCT using a 12-weeks intervention with AET (3x/week, 40 min/session). The study recruited episodic M patients with/without aura (ICHD-II) taking no preventive medicine from an outpatient and a tertiary headache clinic. Primary outcomes were: days with M/month, M attacks/month, and plasma cytokines IL-1β, IL-6, IL-8, IL-10, IL-12p70 and TNF-α (Flow cytometry). Secondary outcomes were: disability, NSAIDs consumption, depression (BDI), anxiety (GAD7), mood (POMS), and VO2Peak. All measurements were conducted interictally.

Results: Twenty female, sedentary participants were randomly allocated to receive AET (EXE, $n = 11$) or enter a waitlist as control (CT, $n = 9$). Groups matched on age and BMI. At baseline, groups matched on clinical status, cytokine levels, and mood. After intervention period, CT showed no significant change at any variable, while EXE showed significant reductions in Days with M/month ($p = 0.001$), M attacks/month ($p = 0.002$), IL-12p70 ($p = 0.036$), GAD7 ($p = 0.034$), and POMS-Depression ($p = 0.005$). There were a positive correlation between changes from baseline in IL-12p70 and days with M ($r = 0.60$, $p = 0.018$), IL-12p70 and Depression ($r = 0.667$, $p = 0.007$), and IL-12p70 and GAD7 ($r = 0.757$, $p = 0.001$).

Conclusion: Our data suggests a new immunomodulatory mechanism for the mood-enhancing and therapeutic effects of AET in M patients involving L-12p70 downregulation.

PO060

Migraine preventive therapy

Half reduction in number of attacks in episodic migraine with left dorsolateral prefrontal cortex repetitive transcranial magnetic stimulation (rTMS). A randomized controlled study

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Background: There are several reports on the role of rTMS in migraine prophylaxis with mixed results.

Aim: Evaluate the role of rTMS in achieving a 50% reduction in the number of attacks in episodic migraine patients.

Method: 33 cases with episodic migraine (more than 4 attacks per month) received 5 successive sessions of left dorsolateral prefrontal (LDLPFC) 5 Hz rTMS at 100% MT(14 active, 19 placebo). They were assessed using a headache diary for one month before and after receiving rTMS. 10 cases were on prophylactic treatment, that was not changed during the study period.

Results: There was no difference between both groups in baseline characteristics. The mean number of attacks was 7.7+/−2.7. There was a 50% reduction in the number of attacks in 69.2% of the active group(9/13) and in 31.25% of the placebo group(4/16) $p = 0.022$. The absolute difference in the number of attacks/month was 3.06 vs 1.45 in the active and placebo groups respectively. Similarly the number of migraine days dropped by 50% or more in 9/13 cases in the active vs 5/16 in the placebo group ($p = 0.048$). There was a 50% reduction in the headache index and number of abortive pills needed in 7/13 and 6/13 cases in the active group respectively but this difference was not statistically significant when compared to the control group.

Conclusion: LDLPFC high frequency rTMS can reduce the number of migraine attacks by 50% or more in almost 70% of a sample of episodic migraineurs.

PO061

Migraine preventive therapy

Surgical deactivation of trigger points in migraine: a case series and the importance of patient selection and surgical technique

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Objective: Assessing the surgical deactivation of trigger point(s) in improving headaches in migraineurs.

Background: Activation of the trigeminovascular system is known in migraine, however, the role of peripheral triggers in this process cannot be ignored. Nerve block/trigger point injections are routinely performed in migraineurs. In the past decade, surgical deactivation of trigger points for migraine headache has been introduced. Trigger points (TPs) are areas where the trigeminal system is being irritated and are detected clinically or radialogically. Main TPs are Frontal, Temporal, Intranasal and Occipital.

Method: A retrospective review of 11 migraineurs (10 female, one male) who underwent surgical deactivation within a two-year period. Pre-surgical screenings were performed by 3 neurologists. All patients meet ICHD-3 criteria for migraine and failed at least 3 classes of preventatives.

Result: Ten out of eleven patients had >50% reduction in frequency and /or intensity of headache within a 3–21 month follow-up period. Two patients had transient pruritus; one patient had wound healing issues.

An interesting observation was the occurrence of aura without headache in two patients.

Conclusion: Central and peripheral factors could activate the trigeminovascular system. In small percentages of migraineurs who have clear peripheral trigger point(s), surgical deactivation could improve headaches.

To improve success rates, patient selection by a headache specialist is critically important. In practice, some centers bypass this step, recruiting patients using less optimal modalities, which may lead to poor outcome.

Proper technical execution for selected TPs requires a well-trained, experienced surgeon.

A multicenter study utilizing correct "selection criteria" is recommended.

PO062

Migraine preventive therapy

Gliacin for the prophylactic treatment of migraine: review of an initial case series

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Background: Migraine is a common primary headache disorder that is often associated with a high level of personal disability. Although used in Ayurvedic medicine for thousands of years, forms of *Boswellia serrata* are relatively new to the headache arena. Gliacin™ is a unique, patent-pending, derivative of *Boswellia serrata* shown to have promise for the treatment of various primary headache disorders.

Aim: Review the cases of ten patients who responded to Gliacin™ for the prophylactic treatment of migraine

Methods: Ten migraineurs (based on the current ICHD) who responded to Gliacin™ (>50% reduction in headache frequency), were followed for a period of three to 24 months. Patients kept daily headache logs and completed monthly HIT-6, MIDAS and Headache Related Quality of Life (HQL) scores for analysis.

Results: Of the responders, eight were female and two were male with ages ranging from 10 to 58 years. The responders' headache frequency dropped from an average of 21 to 2.4 days per month and their average pain level dropped from 7.6 to 4.1 (0 to 10, VAS). Their average HIT-6 score dropped from 70 to 49. Likewise, their MIDAS and HQL sores dropped by 96% (from 81 to 3.4) and 68% (60 to 19) respectively. Only one patient reported side effects (mild dyspepsia).

Conclusions: All migraineurs experienced a reduction in headache frequency, severity and related disability while on Gliacin™. Gliacin™ was well tolerated without any serious side effects. Gliacin™ represents a novel herbal prophylactic that warrants further investigation.

PO063

Migraine preventive therapy

Regulation of TRPM8 expression by inflammatory mediators: implications for novel migraine therapy

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Background: TRPM8 (transient receptor potential melastatin 8) is a menthol-sensitive cation channel that is abundantly expressed in the sensory neurons including trigeminal ganglion neurons. Menthol has been shown to be effective in aborting migraine attacks. More intriguingly, recent GWAS (genome-wide association study) data have disclosed that the *TRPM8* gene is related to susceptibility to develop migraine. Here, we investigated TRPM8 dynamics in expression, intracellular trafficking, and degradation using cell-based assays.

Method: PC12 cells stably expressing an EmGFP-TRPM8-V5 fusion protein were treated with NGF (nerve growth factor) and bradykinin, major inflammatory mediators closely related to pain disorders. Expression levels of TRPM8 protein and transcripts were analyzed by western blot and RT-PCR, respectively. We also checked the effects of pharmacological inhibition for TrkA, JNK (c-Jun N-terminal kinase), p38, MEK (MAPK/ERK kinase), PI3-kinase (Phosphoinositide 3-kinase), and Src. To elucidate the TRPM8 degradation mechanism, proteasome and lysosomal hydrolases were pharmacologically blocked.

Result: TRPM8 expression was up-regulated by NGF in a post-transcriptional mechanism via TrkA. This effect was due to the stabilization of TRPM8 protein after its trafficking to the plasma membrane. Pharmacological analysis revealed that JNK, p38, and PI3-kinase are involved in the TRPM8 trafficking mechanism. As for TRPM8 proteolysis, proteasomal activity played a crucial role.

Discussion: Our results raise the possibility that the NGF-TrkA pathway, JNK, p38, and PI3-kinase can be effective targets for enhancing TRPM8 activity, and provide important information for developing novel migraine therapy based on TRPM8 activation.

PO064

Migraine preventive therapy

A proprietary supplement containing riboflavin, magnesium and Q10 improves migraine symptoms in a randomized placebo-controlled double-blind trial

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Background: Many migraine patients have a decreased level of the micronutrients riboflavin, magnesium and coenzyme in the blood, in cells, and in the brain. Based on this observations a substitution of these micronutrients in migraine patients may reduce migraine attacks.

Aim: The purpose of this trial was to evaluate the efficacy of the commercially available food supplement Migravent® (Dolovent® in the USA) containing a fixed combination of high-dose magnesium, riboflavin and Q10 (along with a multivitamin) for migraine prophylaxis.

Methods: Otherwise healthy adults aged 18 to 65 years of either sex were recruited for this randomized, placebo-controlled, parallel-arm, double-blind prospective multicenter study. The investigational nutritional product was a dietary food for special medicinal purposes containing 400 mg riboflavin, 600 mg magnesium, 150 mg coenzyme Q10 along with a multivitamin per day. After screening, patients underwent a one month baseline period followed by 3 months of treatment.

Results: 112 patients are available for the efficay analysis. The number of migraine days were reduced from 6.2 days to 4.4 days ($p = 0.23$). The intensity of migraine pain was significantly reduced compared to placebo ($p = 0.03$). Migravent® reduced the sum score of the headache impact test questionnaire (HIT-6) by 4.8 points ($p = 0.017$). The evaluation of efficacy by the patient was significantly superior compared to placebo ($p = 0.013$). Adverse events associated with the supplement were mainly abdominal discomfort like diarrhea due to high magnesium amounts.

Conclusion: A fixed combination of magnesium, riboflavin and Q10 in a proprietary nutritional supplement reduced migraine symptoms in the prevention of migraine.

PO065

Migraine preventive therapy

Phase 1, randomized, double-blind, placebo-controlled, single-dose and multiple dose studies of AMG334 in healthy subjects and migraine patients

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Background: Migraines affect >10% of the population worldwide. Calcitonin gene-related peptide (CGRP) plays a role in migraine pathogenesis. AMG334 is a fully human monoclonal antibody against the CGRP receptor.

Aim: To evaluate pharmacokinetics (PK) and safety of AMG334 in single-dose (SD) and multiple-dose (MD) studies of healthy subjects and migraineurs.

Methods: In the SD study, subjects received single, escalating doses of AMG334 (n = 42) 1–210 mg SC, 140 mg IV, or matching placebo (n = 18). In the MD study, subjects received multiple doses of AMG334 (n = 35) 21–280 mg SC or placebo (n = 12) on days 1, 29, and 57. PK and safety were evaluated in both studies; continuous, 24-hour ambulatory blood pressure monitoring (ABPM) occurred in the MD study only. Both studies were approved by the University Hospital Independent Ethics Committee; all subjects provided written informed consent.

Results: After single SC administration, AMG334 exposure increased >dose proportionally from 1–70 mg and ~dose proportionally from 70–210 mg. Median t_{max} ranged from 4–11 days throughout the dose range. There were no apparent differences in PK between healthy subjects and migraineurs. In the MD study, accumulation was ~1.6-fold from doses 1–3. Treatment-emergent AEs were similar in type and frequency between treatment groups and between healthy subjects and migraineurs. No clinically meaningful differences in vital signs or laboratory values were observed. Continuous ABPM demonstrated no change in BP circadian rhythm and no increase in BP with increasing doses of AMG334.

Conclusion: Single and multiple doses of AMG334 were well tolerated with no apparent differences in PK between healthy subjects and migraineurs.

PO066

Migraine preventive therapy

Treatment patterns for migraine patients receiving prophylaxis

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Background: Current treatment options for migraine prophylaxis are associated with poor tolerability, leading to low persistence with treatment.

Aim: To describe prophylactic migraine treatment patterns, including timing, medication type, and duration of use in a large claims database.

Methods: The Truven Health MarketScan® Research Databases were used to identify adults in the US with a migraine diagnosis initiating prophylactic medication (index event) between 2008 and 2011. The following prophylactic medication categories were evaluated: topiramate, beta-blockers, and tricyclic antidepressants. Patients were required to have 12 months of pre- and post-index continuous enrollment.

Results: The overall study population comprised 107,122 patients (Table 1). The mean (SD) age was 41 (12) years and 83% were female. Persistence with migraine prophylactic medication was low; overall, 80% of patients had a gap of >90 days in their migraine prophylaxis in the first year. The gap in therapy occurred early in treatment (mean 95 days), and only 10% of these patients restarted prophylactic therapy within that year. Switching from the index medication to another prophylactic medication or adding prophylaxis was uncommon (13%). At the end of the first year, 65% of patients were not receiving any prophylactic therapy. The percentage of patients receiving any acute medication in the first year was 81%, with opioid use being more common than triptan use (53% vs 48%).

Table 1. Treatment patterns in Migraine patients for 12 months post-initation of prophylaxis

	All Cohorts	Topiramate	Beta-Blockers	Antidepressants
Cohort size, n	107,122	52,275	22,658	32,189
Patients with gap in therapy, %	80%	78%	80%	85%
Time to gap, mean	95 days	102 days	94 days	85 days
Patients who restarted initial prophylaxis after gap, %	10%	12%	9%	9%
Patients not receiving any prophylaxis at year-end, %	65%	62%	63%	70%

Conclusion: Patients with migraine who were initiating prophylactic medication had poor persistence (with early gaps in therapy), relatively infrequent switching, and most discontinued prophylaxis by the end of the first year.

PO067

Migraine preventive therapy

Descriptive comparison of the efficacy and safety of onabotulinumtoxina for headache prophylaxis in adult chronic migraine patients from two long-term, multicenter studies: compel vs. Preempt

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Background: OnabotulinumtoxinA is approved by global regulatory agencies for headache prophylaxis in adult chronic migraine (CM) patients and has had safety/efficacy assessed in numerous clinical studies.

Aim: To compare outcomes between open-label (COMPEL, NCT01516892) and double-blind (PREEMPT, NCT00156910 and NCT00168428) studies at 24 weeks.

Methods: These long-term, multicenter studies in adult CM patients treated with 155U onabotulinumtoxinA every 12 weeks had the same primary endpoint of change in headache days from baseline. Similar secondary measures included change in moderate/severe headache days, headache impact test (HIT-6), and safety. Week 24 data (following 2 treatments) were summarized using descriptive statistics and presented as COMPEL vs. PREEMPT (pooled treatment arm data only).

Results: Enrolled COMPEL (n = 713) and PREEEMPT (n = 688) patients were on average 43 vs. 41 years old; majority were female (85% vs. 88%) and Caucasian (81% vs. 90%). At baseline, patients (n = 691 vs. n = 688) reported an average 21.8 (SD = 4.8) vs. 19.9 (SD = 3.7) headache days/month; 17.8 (SD = 5.7) vs. 17.9 (SD = 4.1) days considered moderate/severe. By week 24, reductions in headache days (−7.6 vs. −8.4 days) and moderate/severe headache days (−6.7 vs. −7.7 days) were observed; HIT-6 scores (−5.4 vs. −4.8 points) showed improvements. Treatment-related adverse events (TRAE) were reported by 15% (n = 106/713) vs. 29% (n = 202/687) patients; 1 serious per study (rash vs. migraine). Most frequently reported TRAE was neck pain (3.2% vs. 6.7%).

Conclusions: Despite differences in study design, the patient population as well as outcomes data from COMPEL and PREEMPT were generally consistent and support the safety and efficacy of onabotulinumtoxinA in CM.

PO068

Migraine preventive therapy

Pharmacokinetic/pharmacodynamic modeling of monoclonal antibody AMG 334 to characterize concentration relationship with capsaicin-induced increase in dermal blood flow in healthy subjects and migraine patients

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Background: AMG 334 is a fully human IgG_2 monoclonal antibody that binds to the human CGRP receptor with high in vitro potency. Inhibition of capsaicin (CAP)-induced increases in dermal blood flow (DBF) has been used extensively as a translational model to characterize the pharmacological effect of CGRP receptor antagonists. This validated model was used to characterize the pharmacological effect of AMG 334.

Aim: To evaluate and quantify the inhibitory effect of AMG 334 on CAP-induced increases in DBF.

Methods: Concentration and DBF-time course data from both single- and repeated-dose studies were pooled for population pharmacokinetic/pharmacodynamic (PK/PD) modeling (Table 1). Both studies were approved by the University Hospital's independent ethics committee. All subjects provided written informed consent. Repeated CAP challenges and DBF measurements were performed within the same subjects, using laser Doppler imaging, over multiple study visits, to estimate the inhibitory effect of AMG 334 on DBF pre- and post-CAP application.

Results: AMG 334 exhibited receptor-mediated drug disposition. AMG 334 significantly inhibited post-CAP challenge DBF, but had no significant effect on pre-CAP DBF. Maximum DBF inhibition was approximately 90%, which was achieved at approximately 1140 ng/mL (Figure 1).

Table 1. Characteristics of Subjects Included in Population PK/PD Modeling

	Single dose N = 52		Repeated dose N = 40	
	Healthy N = 40	Migraine N = 12	Healthy N = 24	Migraine N = 16
Dose regimens	placebo, 1, 7, 21, 70, 140, or 210 mg SC	placebo or 140 mg SC	placebo, 21, 70, or 140 mg SC Q4W x 3 doses	placebo, 21 or 140 mg SC Q4W x 3 doses
Weight (kg)*	80.3 (9.28)	64.5 (11)	75.5 (11.5)	69.2 (14.1)
Age (y)*	26.8 (6.48)	26.2 (9.56)	30.1 (10.3)	32.9 (11.3)
Male/Female (N)	40/0	3/9	23/1	4/12

*Mean (SD); SC = subcutaneous; Q4W = every 4 weeks

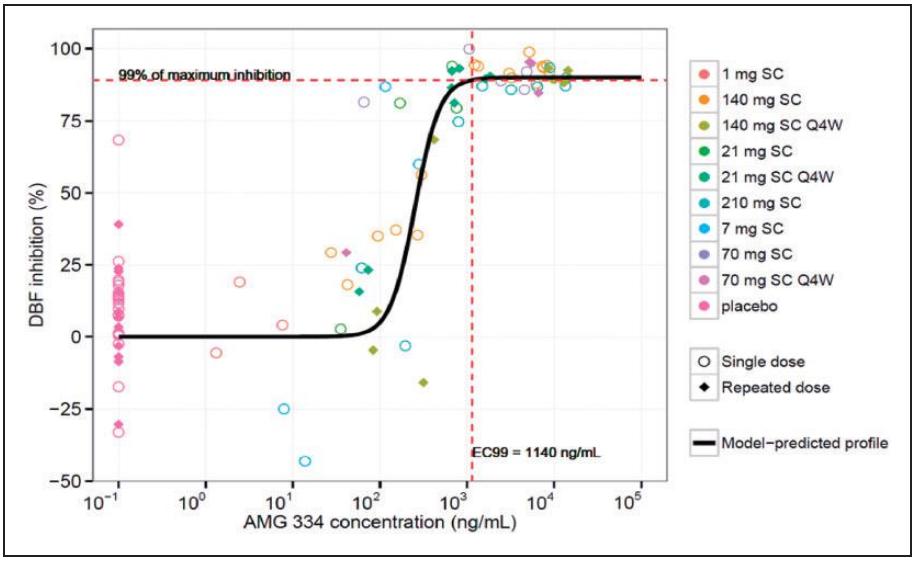

Figure 1. Serum AMG 334 Concentration and DBF Inhibition Relationship

AMG 334 exposure, but not DBF, decreased with increased body weight. No difference in PK and PD were noted between healthy subjects and migraine patients after adjusting for body weight.

Conclusions: AMG 334 administration results in a potent and reproducible inhibition of CAP-induced DBF, indicating complete peripheral CGRP receptor blockade. The favorable PK characteristics translate into a prolonged inhibition of CGRP receptors.

PO069

Migraine preventive therapy

Efficacy, safety, and tolerability of onabotulinumtoxina versus topiramate for chronic migraine prophylaxis in a prospective, randomized, open-label study: forward study methods

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Background: OnabotulinumtoxinA and topiramate have been reported to reduce headache days in chronic migraine (CM) patients. However, there is a lack of

robust evidence comparing the tolerability profiles within the clinical setting.

Aim: Compare efficacy, safety, and tolerability of onabotulinumtoxinA and topiramate for headache prophylaxis in adult CM patients.

Methods: This is a multicenter, randomized, open-label, parallel-group, post-authorization, prospective study (NCT02191579). Patients are randomized to receive 155U onabotulinumtoxinA every 12 weeks or 50–100 mg/day topiramate oral tablets for ≤36 weeks (Figure 1). Patients who discontinue topiramate will receive onabotulinumtoxinA 155U no earlier than 12 and up to 36 weeks. The primary endpoint is proportion of patients with a ≥50% responder rate at week 32. To simulate real-world practice, a worst case imputation method will be utilized; this replaces missing values with baseline values. Thus, if the responder value is missing at week 32 for any reason (eg, discontinuation due to AE, lack of efficacy), then the patient is considered a nonresponder and baseline value will be utilized. Secondary measures include clinical outcomes, patient- and physician-reported outcomes (eg, HIT-6, COWAT, CTS), and safety data.

Results: Target enrollment is 400 patients across ~40 US sites. As of January 2015, 25 sites have been initiated, 12 enrolling, 13 patients randomized.

Conclusions: FORWARD study data may help provide important information regarding the efficacy and safety profiles for these CM treatment options and will help physicians and patients make better informed treatment decisions by setting appropriate expectations.

PO070

Migraine preventive therapy

Atorvastatin versus propranolol in prevention of episodic migraine. A randomized clinical trail

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Background: Prophylactic treatment of migraine isn't ideal. Global efficacy of approved medications is around 60–80%. There are some reports of the efficacy of atorvastatin in patients with hyperlipidemia and episodic migraine. Statins have anti-inflammatory and pleiotropic effects that make them suitable to be tested in migraine.

Methods: We performed a randomized clinical trial to compare atorvastatin versus propranolol in episodic migraine. We included patients with episodic migraine according to current HIS classification in 2013–2014, with 2–6 attacks/month in the previous three months. There was a first washout period (one month), then patients randomly assigned to propranolol (40 mg/d) or

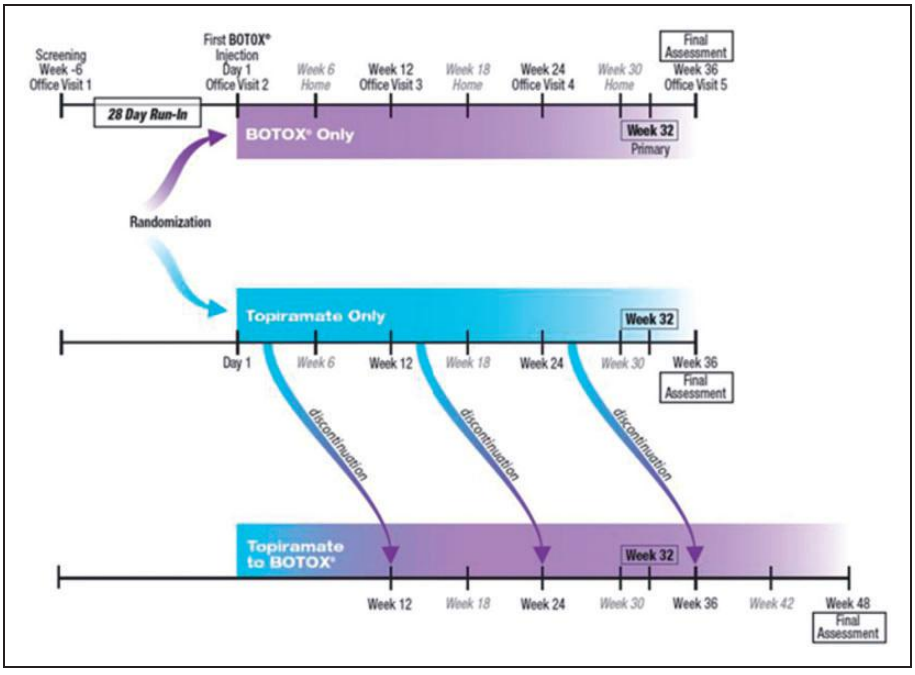

Figure 1. FORWARD Study Design

atorvastatin (40 mg/d) for three months; patients and physicians were blinded to treatment; after another washout period of one month, groups were crossed and received the opposite treatment for 3 more months. We measured number of attacks, pain intensity, MIDAS score, need of rescue medications, global satisfaction with a diary ad hoc.

Results: 26 patients were recruited but only 20 completed the trial. There was no difference in any of the efficacy measures and adverse effects were equal in both groups.

Conclusions: Atorvastatin and propranolol were equally effective and safe in the prevention of episodic migraine. There is justification for a bigger trial.

PO071

Migraine preventive therapy

Characteristics of onabotulinumtoxin-a responder among chronic migraine patients

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Background: OnabotulinumtoxinA is evidence-proven treatment for chronic migraine (CM). We studied the characteristics of OnabotulinumtoxinA –responsive CM patients.

Methods: We prospectively recruited 81 CM patients in a single tertiary hospital, who underwent OnabotulinumtoxinA (155U) injection according to PREEMPT protocol. Seventy-one patients completed the 4-weeks follow up evaluation. Responders were defined as any of following criteria: $\geq$50% reduction from their baseline headache frequency, $\geq$50% reduction of frequency of acute headache pain medication intakes, $\geq$50% reduction of mean headache severity score or improved responsiveness to acute pain medications. We analyzed demographical and radiological findings as well as results of transcranial Doppler (TCD) studies between responders versus non-responders.

Results: A total of 47 patients (66.2%) were classified as responders. Demographics, baseline headache characteristics, comorbidities were not different between responders and non-responders, with a tendency of longer disease duration in non-responders (17.5 [9.46] vs 13.6 [8.28], mean [SD], years. $p = 0.091$). Brain MRI and brain MR angiogram showed no differences between groups. TCD studies demonstrated that the ratio of left MCA/ICA mean flow velocities (MFV) was significantly higher in responders (1.92 [1.60 – 2.60] vs 1.67 [1.43 – 1.97], median [IQR]. $p = 0.021$). The MCA/ICA ratio $\geq$2 were more common among responders than non-responders, in the right side (45.0% vs 15.0%, $p = 0.022$) and either side (56.1% vs 26.3%, $p = 0.045$).

Conclusion: OnatobulinumtoxinA was effective in 66.2% of CM patients. Responders showed a significantly higher MCA/ICA MFV ratio in both the continuous and the categorical analyses. We suggest that TCD findings might be helpful for distinguishing OnatobulinumtoxinA-responders.

PO072

Migraine preventive therapy

Botulinum toxin a for treatment of chronic migraine

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Background: Chronic migraine is a common and debilitating headache syndrome. Botulinum neurotoxin A (BoNT A) has been recently employed for patients suffering from chronic migraine.

Objective: BoNT A has been used in our clinical experience for treating patients suffering from chronic migraine with medication overuse.

Method: A group of 67 patients, suffering from chronic migraine with medication overuse, after withdrawal from medications, have been treated by BoNT A injection in multiple sites according to the PREEMPT protocol study, 155 U for 31 sites, every three months for one year. Number of medication intake and days of headache per month were recorded by a headache daily diary.

Results: Forty six patients at the 3rd session recorded a significant decrease of days of headache /month and medication intake/ month (21.7 ± 6.8 vs 15.6 ± 8.7; 20.3 ± 7.5vs 14.3 ± 8.4). Twenty patients achieved the last (5th) session of treatment: days of headache /month and medication intake decreased too (although not significantly) (pre 22.4 ± 6.5 vs 13.8 ± 7.4 $p < 0.0005$; 20.7 ± 7.2 vs 16.4 ± 18.6). Five patients asked for additional treatment.

Conclusion: Although these results are preliminary they led to intense efforts to evaluate analgesic properties of BoNT A and to assess its clinical applicability. The pharmacological profile of BoNT A makes it a good candidate for migraine prevention. Its long duration of action (3 months)

makes it particularly attractive for patients who are not compliant with the daily use of preventive medications, or if they cannot tolerate them or when they are refractory to preventive medications.

PO073

Migraine preventive therapy

Multidisciplinary treatment for chronic migraine with medication overuse: preliminary study

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Introduction: The problem concerning treatment of patients with chronic migraine (CM) associated to medication overuse (MO) is challenging in clinical practice. A single modality of treatment, as pharmacological prophylaxis, can be insufficient for these patients. Nowadays, withdrawal is considered the most adequate procedure to help these patients to stop the vicious circle between medication and pain, nevertheless, after that, usually they are not adequately followed and the pharmacological prophylaxis don't help them to avoid relapses in overuse.

Methods: Nineteen female patients (mean age 44.2 ± 6.8) suffering from Chronic Migraine with Medication Overuse (diagnosis according with IHS criteria) were submitted to a withdrawal in a day hospital setting. Then, a multidisciplinary treatment including: pharmacological prophylaxis, physical activity schedule (twice per week), cognitive-behavioral approach (6 sessions of relaxation training combined with mindfulness practice, twice per month and home practice) was performed. Daily Headache diary was given to record headache attacks and medication intake. MIDAS Questionnaire was performed before treatment and at the follow-up.

Results: At one-year follow up, patients improved from the clinical point of view: days of migraine/month and medication intake/month decreased significantly (23.4 ± 6.6; at 12 months 11.7 ± 8.3; 18.1 ± 4.4 pre; at 12 months 8.8 ± 4.3 respectively). MIDAS total score decreased too (82.2 ± 75.4 pre vs 43 ± 55.2 at 12 months).

Conclusions: Although the study lack of a control group or a comparison condition, data obtained suggest that a multidisciplinary strategy seems to be a good option to manage patients with CM and MO instead of pharmacological treatment only.

PO074

Migraine preventive therapy

Safety considerations may explain migraineurs' choice of 'alternative' treatments

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Background: The growing interest in complementary/alternative medicine (CAM) is a worldwide phenomenon. Headache and migraine are among the top five conditions treated with such therapies, despite the scarcity of scientific proof.

Objective: To explore Hungarian migraineurs' opinions about CAM use. Method: Questionnaire survey of migraineurs, conducted at 3 headache centres. We used Chi-square tests for the differences between groups or treatment scenarios.

Results: 112 migraineurs (mean age: 35.6 ± 12.0 years; 103 women) were enrolled. Forty-nine (44%) had already tried at least one CAM. Previous CAM use was higher among patients with higher levels of education ($p < 0.0001$). Eighty percent of the patients would be willing to pay for CAM recommended for their migraines, on average 16% of the Hungarian monthly net minimum wage. If scientific evidence of efficacy was lacking, 51% of the patients would pay for CAM (on average 12% of the net minimum wage). If CAM were associated with side effects, only 32% of patients would try them. Of two equally effective therapies, 62% of migraineurs would choose a CAM and 13% would prefer a conventional treatment (25% having no preference); if the two treatments' side effects were equal, only 42% would choose the CAM, 19% the

conventional treatment, and 39% would have no preference ($p = 0.0153$ for the difference between the two scenarios).

Conclusion: The majority of migraineurs had positive attitudes towards CAM. This is probably due to CAM being considered safer than conventional therapies. Patients with higher levels of education more readily use CAM.

PO075

Migraine preventive therapy

Sustained response outcomes from a phase 2a, randomized, double-blind, placebo-controlled study of LY2951742, a monoclonal antibody to calcitonin gene-related peptide, for the prevention of migraine: a post-hoc analysis

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Background: At the endpoint of a recently reported study of LY2951742 vs. placebo various levels of response are reported. Two important clinical issues include how long positive responses are maintained, and whether a positive response occurs in initial non-responders at 1 month.

Aim: We sought to examine sustained response outcomes for month 1 responders, and to determine subsequent response outcomes for non-responders at month 1.

Methods: Post-hoc analyses from a phase 2a proof-of-concept study in patients aged 18–65 years with 4 to 14 migraine headache days per month who were randomly assigned to LY2951742 or placebo (NCT01625988) identified the proportion of patients with $\geq$50%, $\geq$75%, and 100% reduction in migraine headache days from baseline at month 1 who sustained those response levels for month 2 and month 3 (defined as 'sustained response"). For non-responders at month 1, the proportions of patients with $\geq$50%, $\geq$75%, and 100% response at month 2 and 3 were identified.

Findings: A total of 217 patients were randomized and received LY2951742 ($n = 106$) or placebo ($n = 110$). The proportion of LY2951742- vs. placebo-treated patients meeting $\geq$50%, $\geq$75%, and 100% sustained response were 47% vs. 25%, 22% vs. 13%, and 11% vs. 2%, respectively. Subsequent response outcomes for non-responders at month 1 will be reported.

Conclusion: These post-hoc analyses further characterize response outcomes from a single phase 2a trial of LY2951742 in migraine prevention. It is encouraging for patients and physicians that a significant proportion of responders continue their improvement out to three months.

PO076

Migraine preventive therapy

Previous use of migraine prophylaxis and consultation of health professionals in a cohort of 200 migraineurs

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Background: Access to medical care, including prophylaxis, is limited for migraineurs. Patients may seek the help of other health professionals (HP), but the efficacy of alternative techniques is often poorly documented.

Aim: To determine previous patients' experiences with health professionals for treatment of their migraines and the subjective benefits of these interventions.

Methods: We studied a cohort of 200 migraineurs newly referred to our centre. A questionnaire was filled about past consultations for migraine with HP and the benefits of these approaches was retrospectively assessed by patients on a Likert scale.

Results: 197 patients filled the questionnaire. There were 88% women and the mean age was 40 years old with a standard deviation of $\pm$13 years. The monthly frequency of attacks was 1–6 (episodic, 22,3%), 7–14 (frequent episodic, 45,2%), and 15 or more (chronic, 32,5%). Prophylaxis had never been prescribed in 47,6% of frequent episodic patient and 18,8% of chronic patients. Health professionals consulted for migraines included massage therapist (41,5%) osteopath (40,0%), acupuncture therapist (39,5%), chiropractor (35,0%), physiotherapist (21,0%), psychotherapist (17,5%), and nurse (7,0%). 31,0% of

patients had consulted 3 HP or more for their migraines. The consultation of HP was associated with the number of prophylactics tried ($p = 0,02$). The benefit of the HP interventions was described as very helpful (29,9% to 52,8%) or not helpful (33,3% to 61,8%).

Conclusion: A significant portion of patients with frequent migraines do not receive prophylactics. Migraineurs tend to seek the help of health professionals but the subjective benefit of these techniques is variable.

PO077

Migraine preventive therapy

A survey of UK practitioners on the use of botulinum toxin a in pregnancy

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Background: Botulinum toxin A (BtxA) has a wide range of medical and non-medical indications for its use. Medical indications include management of chronic migraine, spasticity, and dystonia for example. Data on its use during pregnancy remains limited.

Aim: This study aimed to survey BtxA use in pregnant women with neurological indications and the attitude of its use among injectors.

Method: Questionnaires were sent to members of the British Association for the Study of Headache (BASH) and the Association of British Neurologist Special Interest Movement Disorders Group in the U.K which included a proportion of injectors. These practitioners were asked a number of questions including an approximate number of patients they had administered BtxA to and the neurological indications for its use. They were also asked whether they had knowingly or unknowingly administered BtxA in pregnancy and the outcome. Finally there were asked how comfortable they were with the use of BtxA during pregnancy.

Results: Forty-nine responses (13.5%) were received of the 362 practitioners surveyed. 100 percent of responders had injected BtxA for a neurological indication. Thirteen (25%) of the respondents had administered BtxA in pregnancy. Twenty-nine patients were injected during pregnancy across all trimesters, one of which was a twin pregnancy. One miscarriage and one premature birth were reported which is within background average statistics. All other pregnancies were uneventful. Eighteen (36.7%) respondents admitted to being comfortable with administering BtxA in pregnancy.

Conclusion: Further data is required about the safety of administering BtxA in pregnancy but initial results appear encouraging.

PO079

Migraine preventive therapy

Safety and efficacy of botulinum toxin for chronic migraine in the elderly

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Background: Among elderly, polypharmacy is a common risk factor for adverse drug events. Currently onabotulinumtoxinA is the only FDA approved therapy for headache prophylaxis in adults with chronic migraine (CM) but not for people over the age of 66. There is limited data in the safety and efficacy of onabotulinumtoxinA in the elderly population.

Objective: To evaluate the efficacy and safety of onabotulinumtoxinA for prophylaxis of headaches in patients 66 years old or older meeting the IHC diagnostic criteria of CM.

Methods: A chart review of 64 patients of target age with a diagnosis of CM receiving treatment cycles of 100–175 units given at 12-week intervals. Data was analyzed from questionnaires filled out prior to each visit regarding the intensity and number of headache days per week and any side effects from onabotulinumtoxinA. Only patients doing well on 100 units prior to FDA approved paradigm remained on this dose.

Results: The responder rate (reduction of headache days per month more than 50%) was 85.6% at 12-weeks post cycle and 6.2% had complete remission. On average, the number of headache days was reduced by 60%, and the intensity was reduced by over 50%. Fourteen percent did not have any improvement in symptoms. Eyebrow ptosis and neck pain were the most common side effects.

Conclusion: OnabotulinumtoxinA injections at doses of 100–175 units administered every 12 weeks is well tolerated and effective for the prophylaxis of headache in elderly with CM making it ideal in this population with polypharmacy and multiple comorbidities.

PO080

Migraine preventive therapy

Long-term experience with onabotulinumtoxina in the treatment of chronic migraine: lessons after one year

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Background: OnabotulinumtoxinA (onabotA) is efficacious in chronic migraine (CM), but trials lasted one year.

Objective: To analyse our experience with onabotA but paying attention to what happens after one year.

Patients and Methods: We reviewed the charts of CM patients on onabotA. Patients were injected quarterly during the first year but the fifth appointment was delayed to the fourth month to explore the need of further injections.

Results: We treated 132 patients (mean age 47 years; 119 women). 108 (81.8%) responded during the first year. Adverse events, always mild, were seen in 19 (14.4%) during the first year; two showed frontotemporal muscle atrophy after >5 years. The mean number of treatments was 7.7 (limits 2–29). Among those 108 with treatment >one year, 49 (45.4%) worsened prior to the next treatment, which obliged us to return to quarterly injections and injections were stopped in 14: in 10 (9.3%) due to lack of response and in 4 due to attack disappearance. In responders, after 2 years of treatment, consumption of acute medication was reduced by 53% (62.5% in triptan overusers) and emergency visits decreased 61%.

Conclusions: Our results confirm the long-term response to onabotA in three quarters of CM patients. After one year, lack of response occurs in one out of ten patients and injections can be delayed, but not stopped, to four months in around 40%. Except for local muscle atrophy in two cases treated more than 5 years, adverse events are comparable to those in short-term trials.

PO081

Migraine preventive therapy

Onabotulinumtoxina decreases interictal CGRP plasma levels in chronic migraine patients

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Background: OnabotulinumtoxinA (onabotA) has shown efficacy in chronic migraine (CM). Its mechanism of action, however, remains obscure.

Objective: We have analysed whether treatment with onabotA is able to induce changes in interictal plasma calcitonin gene-related peptide (CGRP) concentrations, which have been shown to be increased in CM patients. Patients and Methods: CGRP levels were determined in samples obtained from the right antecubital vein by ELISA, outside a migraine attack and having taken no symptomatic medication in the previous 24 h, in 83 CM patients (average age 44 years; 94% females) before and one month after treatment with 155–195 U of onabotA. CGRP levels after onabotA treatment (median 51.89 pg/ml; range 199.4–10.2) were significantly decreased as compared to CGRP levels obtained before onabotA treatment (median 74.09 pg/ml; range 241.0–11.4; $p = 0.001$). Pretreatment CGRP levels in responders (76.85 pg/ml) were significantly higher than those seen in nonresponders (50.45 pg/ml; $p = 0.001$). One month after treatment, CGRP levels did not change in nonresponders (51.89 pg/ml; $p = NS$), but significantly decreased in responders (52.48 pg/ml; $p = 0.003$). A number of demographic factors, clinical features and comorbidities were not different in responders as compared to nonresponders.

Conclusions: These results confirm that interictal CGRP levels can be of help on predicting the response to onabotA and suggest that the mechanism of action onabotA in CM is the reversal of sensitization as a result of the inhibition of CGRP release.

PO082

Migraine preventive therapy

A single dose, placebo-controlled, randomized, ascending dose study of ALD403, a humanized anti-calcitonin gene-related peptide monoclonal antibody administered IV or SC – pharmacokinetic and pharmacodynamic results

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Background: CGRP is involved in the pathophysiology of migraine. We evaluated the pharmacokinetics and pharmacodynamics of ALD403, a humanized anti-CGRP antibody, in healthy subjects.

Methods: The trial was approved by the Institutional Review Board and conducted in accordance with applicable ICH GCP guidelines. All subjects signed a written informed consent. Ascending dose levels of ALD403 ranging from 1 to 1000 mg or placebo were administered intravenously or subcutaneously to healthy male or female subjects. Plasma samples were collected, analyzed for Free (unbound) ALD403 concentration, and pharmacokinetic results were generated according to standard non-compartmental methods. Pharmacodynamic effects following ALD403 administration were investigated by evaluating the inhibition of vasodilation induced by topically applied capsaicin solution to the forearm. The exposure-response relationship was explored utilizing a nonlinear mixed-effects (NLME) population pharmacodynamic model.

Results: The pharmacokinetics were dose proportional with respect to C_{max} and AUC_{inf}. The C_{max} was attained soon after the intravenous delivery of ALD403 and the mean plasma half-life ($t_{1/2}$) was approximately 26 days. The mean CL and Vz remained relatively constant and ranged from 6 to 8 mL/hr and 4.8 to 7.2 liters, respectively. The bioavailability for subcutaneously administered ALD403 was 70%. Subjects receiving ALD403 had dose-dependent reductions in mean % baseline capsaicin/vehicle dermal perfusion ratios relative to placebo.

Conclusions: The pharmacokinetic results for ALD403 were consistent with the expectations for a humanized monoclonal antibody. Reductions in capsaicin induced dermal perfusion occurred following single administration of 30 to 1000 mg ALD403 and persisted for 12 weeks.

PO083

Migraine preventive therapy

Onset of efficacy of LY2951742 in migraine prevention: post-hoc analysis of phase 2a, randomized, double-blind, placebo-controlled study data of a calcitonin gene-related peptide monoclonal antibody

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Background: Despite the availability of preventivemedications for migraine, significant needs remain for efficacious andtolerable new medications. Their development offers opportunities to askclinically relevant questions, such as when efficacy of a novel preventive starts.

Aim: Use a post-hoc analysis from a positiveclinical trial to determine the time to onset of efficacy of LY2951742, ahumanized monoclonal antibody to calcitonin gene-related peptide, for the preventionof migraine.

Methods: Theseanalyses were conducted using data from a randomized, double-blind,placebo-controlled, phase 2a study in patients aged 18–65 years with 4 to 14migraine headache days per month who were randomly assigned to LY2951742 orplacebo for 12 weeks (NCT01625988). To assess the onset of efficacy, daily data reflecting if the patient had amigraine headache ("yes" vs "no") during the 12-week treatment period wereaggregated into the number of migraine headache days for each weekly interval. Onset of efficacy was defined as the first week in which LY2951742 wasstatistically superior to placebo in reduction of migraine headache days perweek.

Findings: In analyses of both migraine headachedays (MHD) and probable MHD, the onset of efficacy of LY2951742 ($n = 106$) wasobserved as early as week one compared with placebo ($n = 110$). LY2951742continued to demonstrate statistically significant improvement compared withplacebo at the majority of subsequent weeks including endpoint (week 12) forMHD, but not probable MHD at endpoint compared with placebo.

Conclusion: These analyses suggest evidence of onsetof efficacy of LY2951742 as early as week one.

PO084

Migraine preventive therapy

Environmental stress and spreading depression

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Background: Stress has been suggested as a factor that modulates the likelihood of migraine attacks. Mechanisms are poorly understood. Cortical spreading depression (CSD) is the electrophysiological event underlying migraine aura, and likely headache.

Aim: To test whether environmental stress or its removal modulates CSD susceptibility.

Methods: Wild type (WT) and familial hemiplegic migraine type 1 (FHM1, S218L) heterozygous knock-in mice were subjected to acute, chronic stress, or chronic stress and withdrawal. Acute stress was induced by restraint, and exposure to bright lights and loud white noise for 3 hours. Chronic stress was induced for 28 days via exposure to rats (days 1–7 and 15–21), restraint (days 8–10 and 22–25), and forced swimming (11–14 and 26–28). In a separate cohort, chronic stress was followed by withdrawal for 36 h. CSD susceptibility (electrical CSD threshold and 300 mM KCl-induced CSD frequency) was determined in the cortex at the end of each protocol.

Results: Neither acute nor chronic stress significantly affected CSD susceptibility (threshold, frequency, or propagation speed) in FHM1 mutants or WT ($n = 14$–17). Following withdrawal of chronic stress, FHM1 mice showed a 30–40% increase in SD frequency when compared with both naive ($p < 0.05$) and stressed ($p < 0.001$) mutant mice with no withdrawal ($n = 9$–14).

Conclusions: Our studies suggest that stress, acute or chronic, does not significantly affect SD susceptibility in WT or FHM1 mutant mice. However, its withdrawal for 36 h enhances CSD susceptibility in FHM1 mutants. This finding is clinically congruent with the propensity of migraine attacks after relief from stress.

PO085

Migraine preventive therapy

Type-A botulinum toxin treatment for chronic migraine with and without anxiety and depression disorders comorbidity in a multidisciplinary setting

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Background: Type-A Botulinum Toxin (BoNTA) therapy for Chronic Migraine (CM) response varies. Psychopathological comorbidity and its management might play a role in this variability.

Aim: The study compares responders and non-responders to BoNTA treatment for CM regarding to psychosocial variables.

Method: 26 CM patients (6 males; 20 females) from 33 to 61 years old aged (M: 47.46) were treated in a multidisciplinary setting with 100-units BoNTA injections. Sessions occurred once every 3 months from January 2014 to January 2015; patients received psychological counselling and education; headache frequency, pain intensity, disability, anxiety and depression levels were assessed using clinical interviews, headache diary and psychometric tests at the baseline and at final follow-up. Patients were divided into responders ($\geq$50% reduction in headache frequency and/or pain intensity compared with baseline) and non-responders ($<$50% reduction in in headache frequency and/or pain intensity compared with baseline). Descriptive and hypothesis tests were performed to explore the relationship between psychosocial information and clinical outcomes.

Results: 64.51 % of patients were responders to BoNTA and significant reduction treatment effect was observed regarding frequency ($p < 0.05$), anxiety ($p < 0.001$), depression ($p < 0.001$) and disability ($p < 0.05$). A greater percentage of psychopathology comorbid patients than non-comorbid responded to treatment (80% $>$ 50%) while a significant effect of comorbidity was not found.

Conclusions: BoNTA in a multidisciplinary setting might be an effective treatment for CM and headache-related affective disorders. Outcomes might be linked to central mechanisms and multidisciplinary interventions. Larger randomized and controlled studies might clarify those aspects.

PO086

Migraine preventive therapy

Understanding reasons for patient non-adherence to prophylactic migraine medications

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Background: Literature shows that migraine prophylactics are associated with poor adherence but reasons for non-adherence are not well understood.

Objective: To evaluate factors leading to non-adherence with migraine prophylactics.

Methods: A literature review was conducted using terms related to migraine, prophylaxis and adherence. Qualitative, semi-structured interviews were then conducted with 3 migraine clinical experts to solicit feedback on literature review results and to inform development of a patient focus group discussion guide. Three focus groups with episodic or chronic migraineurs recruited from different US locations were conducted to elicit patient accounts of experiences with migraine prophylactics using the discussion guide.

Results: Based on the 21 studies reviewed, most frequently cited reasons for non-adherence were medication-related side effects, frequent/complex dosing regimen, perceived poor efficacy, administrative/financial burden, and prophylactic medication type. Clinicians interviewed reported side effects/tolerability as the most prominent factor for migraine prophylactic non-adherence. Analysis of focus groups with episodic and chronic migraineurs ($N = 20$) revealed two types of non-adherence: accidental (forgetting to take medication) and intentional non-adherence (intentionally changing dose/timing of medications prior to consulting physician). Reasons for intentional non-adherence included side effects, perceived medication effectiveness and/or ineffectiveness, and administrative burden. Participants ranked side effects as the most disliked features of migraine prophylactics, followed by daily administration, feeling dependent on/stigmatized by the prophylactic, financial/administrative burden, and perceived ineffectiveness.

Conclusions: This study confirms that the primary reason for medication non-adherence is side-effects associated with current prophylactics. This is consistent from different sources of information, literature reviews, clinician interviews and patient focus groups.

PO087

Migraine preventive therapy

Effect of pranayama & relaxation technique (yoga therapy) on migraine: a clinical & autonomic function study

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Background: Migraine is a highly prevalent neurological disorder which has multiple clinical manifestations including autonomic symptoms. Pranayama & Relaxation Technique (Yoga) is traditional Indian psycho-philosophical-cultural method. Yoga can be one of the best preventive therapy which has multiple health benefits and can influence on sympathovagal balance.

Aim: To study the effect of Pranayama & Relaxation technique (Yoga therapy) on clinical & on Heart rate Variability (HRV) in migraine patients.

Methods: Twenty chronic migraine patients (age 34.40 ± 7.4 yrs) fulfilling the International classification of headache disorders (ICHD) II criteria, were recruited from the Neurology outpatient department and written consent was taken. Patients were randomized to receive conventional treatment with structured Pranayama & Relaxation techniques practiced daily 30 minutes for 30 days(Yoga group, $n = 10$). While the other group received conventional treatment only for migraine (control group, $n = 10$). Assessments were carried out before and after yoga therapy using HRV for cardiac autonomic function, headache impact test (HIT), visual analogue scale (VAS) for pain. HRV was analysed offline with Lead II resting ECG

which was recorded for 15 minutes. Data were analysed by Independent sample't' test.

Results: Following yoga therapy, patients exhibited significant improvement in Cardiac autonomic function (LF $p = 0.000$; HFnu $p = 0.001$ & LF/HF ratio $p = 0.001$) and clinical parameters (HIT pre 75.7 ± 5.33;post 43.40 ± 6.38, $p = 0.000$; VAS pre 9.2 ± 0.63, post 2.30 ± 0.67, $p = 0.000$) in yoga group when compared to control group.

Conclusion: Our study shows that Pranayama & Relaxation technique enhanced the vagal tone and reduced the frequency and intensity of headaches, thus improving the quality of life.

PO088

Migraine preventive therapy

Short-time prophylactic treatment – first step in management of patients with chronic primary headaches

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Background: Chronic primary headache, often co-existed with comorbid conditions and medication overuse headache, is a remarkable medical and socio-economic problem.

Aims: We tried to find the best therapeutic intervention for patients with chronic primary headache at the moment they attend headache specialist.

Methods: In a sample of 130 out-patients with primary headaches,adults and both genders, according to diagnostic criteria of ICHD-III and headache diary – chronic migraine and chronic tension type headache (TTH) were diagnosed. After withdraw of previous analgesics we started with naproxen-Na (recommended in migraine prophylaxis by Guideline of EFNS): 550 mg tablet in the morning, 20 days. During the 6 months follow-up period weevaluated the therapeutic efficacy of that schedule.

Results: In our sample, age 18–65 years, males 29 (22.3%), females 101 (77.7%), there were 95 patients with migraine(73.08%) and 35 with TTH (26.92%). There were 63 patients (48.46%) with chronic primary headache, with migraine 41/63 (65.08%) and with TTH 22/63 (34.92%). The reduction of $>= 50\%$of headache days per month was achieved in 49/63 patients (77.77%), 36/41 with migraines (87.80%) and 13/22 with TTH(59.09%). That therapeutic benefit continued next 4–8 weeks and afterwards, when necessary, we prescribed a long-term prophylactic drug.

Conclusions: There was a clinically relevant therapeutic benefit of short-term prophylactic treatment with naproxen-Na 550 mg tb., in patients with chronic headaches, particularly in those with migraine. The main advantages of this treatment are to helpheadache patients immediately and to motivate them to persist in the effort of headache management.

PO089

Migraine preventive therapy

Optimizing treatment effects of occipital nerve stimulation by adjusting stimulation parameters in the treatment of chronic migraine

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Aim: Occipital Nerve stimulation (ONS) is used for treating therapy-resistant chronic migraine. The relationship between stimulation parameters, induced sensations and the clinical efficacy of treating migraine is widely unknown to date. Therefore, the aim of this study is to evaluate the relationship beween stimulation parameters, sensations induced by ONS and clinical treatment effects.

Methods: 31 patients treated by ONS, were included in our study in the time period from November 2011 to January 2015. We used a new computer-based imaging method (Göbel et al. 2014) for mapping the spatial, cognitive and affective sensory effects of ONS. We analyzed 808 individual quantitative and qualitative data sets of the relationship between lead positioning, the stimulation settings as well as the sensory and clinical stimulation effects.

Results: Sensations induced by ONS below the line connecting the external acustic meati with the occipital protuberantia (MOP) show no relationship with migraine treatment outcome. However, a highly significant relationship exists between clinical efficacy, stimulation parameters

(intensity, volume extension, quality and pleasantness of sensation) for induced paresthesias above the MOP line. 48.9% reported that the global effect of ONS stimulation was moderate to very good, 44.6% reported a weak and 6.1% reported no effect.

Conclusion: Lead positioning, the stimulation settings as well as the sensory and clinical stimulation effects are of essential importance for clinical efficacy. Sensations induced by ONS above the MOP line are essential for significant clinical effects. The efficacy of ONS can be individually optimized when these results are considered.

PO090

Migraine preventive therapy

Treating chronic migraine with botulinum toxin Type A (BTX-A) – do affective disorders influence 12 month outcome?

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Background: Depression and anxiety are common comorbid disorders of migraine. We examined the influence of affective symptoms on outcome of BTX-A in Chronic Migraine.

Aim: To describe the proportion of severe headache days at 12-month follow up, and the influence of affective symptoms.

Methods: Headache diaries, Anxiety/Depression Scales (HADS, GAD-7 and PHQ9) were prospectively administered during routine care of 83 consecutive patients attending for BTX-A. Primary Outcome – change in proportion of diary days with severe headache (7–10 on a 0–11 scale). Ethics approval was not required as this work is part of a service evaluation programme.

Results: Since 2011 we administered BTX-A to 83 people with Chronic Migraine. Prospectively completed headache diaries contained data on 3724 days (0 m) and 5106 days (12 m). Anxiety and Depression rating scales were completed by 58. The proportion of severe headache days reduced from 60% (0 m) to 34% (12 m). There was no statistically significant difference in the reduction of severe headache days between those who were Anxious (56% to 34%, n = 23), Borderline Anxious (73% to 40%, n = 8) or Non-Anxious at 12 months (55% to 33%, n = 27), nor between those who were Depressed (64% to 39%, n = 28), Borderline Depressed (50% to 39%, n = 10), or Non-Depressed (58% to 28%, n = 20).

Conclusions: Meaningful reductions in severe headaches occurred in 83 people with Chronic Migraine over a 12-month period, but were not influenced by the presence of an affective disorder.

PO091

Migraine preventive therapy

Use of physiotherapy by 83 people with chronic migraine undergoing treatment with botulinum toxin Type A (BTX-A)

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Background: Neck pain is an independent epidemiological risk factor for severe headache. We reviewed use of physiotherapy in people with Chronic Migraine attending for BTX-A.

Aim: To compare CM outcomes between physiotherapy prior, during, or not at all during BTX-A treatment.

Methods: Prospective Headache Diaries of 83 consecutive BTX-A treated patients. Retrospective chart review for physiotherapy information. Primary Outcome – change in proportion of diary days with severe headache (7–10 on a 0–11 scale).

Results: 63/83 (76%) people had physiotherapy (42 during and 21 prior) and 17 did not. Severe headache days fell from 60% (0 m) to 34% (12 m) in all 83 people. There was no statistically significant change in severe headache days between physiotherapy (76% at 0 m to 37% at 12 m, n = 63) and no physiotherapy (56% at 0 m to 33% at 12 m, n = 17). People with physiotherapy prior (n = 21) had a trend towards more frequent pain free days (10% at 0 m, 37% at 12 m) compared to no physiotherapy (1% at 0 m, 21% at 12 m, n = 17) or physiotherapy during treatment (5% at 0 m, 19% at 12 m, n = 42).

Conclusions: We found a trend towards lower pre-treatment pain levels and more pain free days in those with physiotherapy prior to BTX–A. The role of physiotherapy in Chronic Migraine could be explored in larger, controlled, prospective studies as a clinically meaningful treatment effect may be present.

PO092

Migraine preventive therapy

Changes in vasoreactivity and molecular biomarkers in response to anhydrase carbonic inhibitors. A prospective study on chronic migraine

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Background: Previous studies report changes in vasoreactivity in migraine patients. Transcranial Doppler enables dynamic assessment of these changes. New biomarkers than should facilitate diagnosis have been discovered but its relationship to chronic migraine (CM) and its response to treatments remains misunderstood.

Aim: To determine changes in potential biomarkers and vasoreactivity for CM, previously and during treatment with carbonic anhydrase inhibitors (CAI) and the presence of predictive factors for therapeutic response.

Methods: Patients with CM according to ICH-2004 and 2006 criteria were recruited and informed consent was obtained. Studies were carried out in fasting subjects, previously, 1 and 3 months after starting treatment.

Ultrasonography images were obtained according with ultrasounds protocol. The vascular parameters of both medial cerebral arteries and basilar artery were recorded. Vasoreactivity was measured using the Breath Holding Index (BHI). Flow mediated dilatation (FMD) was measured by assessment of changes in brachial artery diameter after a vasodilatation stimulus.

Blood samples were drawn in each visit for biochemical analysis and RNA study of biological markers related to migraine. Statistics were obtained with SPSS v.15.

Results: So far, we have recruited 20 patients. BHI values increase in patients who respond to CAI and there are no changes in those with treatment failure ($p = 0{,}025$). FMD increases over the treatment in cases of effectivity ($0{,}05 < p < 0{,}1$). We have also observed changes in biological markers over the treatment.

Conclusions: CAI could normalize the vasoreactivity changes observed in migraine. Changes could be explained by the influence of inflammatory biomarkers in migraine.

PO093

Migraine preventive therapy

Attention deficit and hyperactivity disorder and response to stimulants in chronic migraineurs

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Chronic Migraine (CM) sufferers often present psychiatric comorbidity, mainly mood and/or anxiety disorders, being more difficult to treat. Attention Deficit and Hyperactivity Disorder (ADHD) appears not only in children but also in adults. ADHD overlaps with bipolar and anxiety disorders in the adult population and can be easily misdiagnosed. We report 12 patients with ADHD and CM diagnosis who were started in a stimulant therapy. DSM-IV and IHS criteria were met. Other patients were also diagnosed but excluded from the stimulant therapy because of bipolar disorder diagnosis, hypertension, previous history of drug abuse, previous stimulant use, insomnia, panic disorder, BMI lower than 18, and glaucoma. Patients started lysdexamfetamine 30 mg, doses were escalated if necessary, either for headache or ADHD control. Two patients did not tolerate and stop the medication, one due to worsening of headaches and other excessive irritability. The median dose was 50 mg. At least a mild improvement in ADHD and headache were observed in all 10 patients. Four patients had more than 90% decrease in headache frequency, 4 50–90%, and 2 had less than 50% improvement. All patients had poor response to previous preventive treatments. Eight patients also reported significant improvement in anxiety levels. Weight loss occurred in all patients. ADHD may coexist with CM, if suspected, a stimulant trial most likely result in better headache control and ADHD improvement. Further trials are necessary to assess the risk and benefit of stimulant therapy in migraine and ADHD and co-existing insomnia, bipolar spectrum, and anxiety disorders.

PO094

Migraine preventive therapy

Yokukansan and lomelizine was effective in the case of MOH

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Background: It is necessary to start preventive medicine when we treat medication overuse headache (MOH) patient. We would like to report a case both yokukansan and lomelizine was effective to MOH patients. She could recover within a weak after we prescribe yokukansan and lomelizine.

Case: 21 years old female

Cc: Headache

Ph: Mother suffered from migraine without aura.

O/C: She felt headache from her high school days. First she had a throbbing pain with photophobia and phonophobia once a month. In her junior college days the frequency of headache was increased. After the graduation, headache attack was transformed. Following her father's sudden death, headache character was transformed. She felt headache every day and she took OTC every day for more than 6 months. But the effect of OTC was getting weak. We changed OTC to acetaminophen and start to treat with lomelizine. She didn't want to VPA, triptanol, or propranolol because of their side effects. We prescribe yokukansan with lomelizine. The patients could easily quit taking OTC within a weak. We treated her with lomelizine and yokukansan for a month. One month later, the headache attack was becoming episodic.

Discussion: Yokukansan was tried to babies who cried during midnight in 9th century. These days, yokukansan is prescribed for BPSD, neuralgia or anxiety in Japan. In this case, as transformation of headache was associated with an anxiety after her father's death, yokukansan should be effective for such an anxiety. It is suggested in the experiments that yokukansan regulates glutamic acid metabolism and changes the threshold of pain. So Yokukansan might be effective to MOH as a kind of preventive medicine.

PO095

Migraine preventive therapy

Intensity and frequency are the strongest predictors of treatment efficacy after Botox®: design of a migraine treatment assessment scale (gain scale)

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Aim: To design a weighted scale to assess Botox® treatment response.

Method: We included patients with more than 10 headache days/month who received 2 cycles of Botox®. Data regarding migraine characteristics before and after Botox® were collected: headache frequency, intensity, duration and analgesic use. Good responders were considered when an improvement of $\geq$50% in $\geq$2 items was observed. A multivariate logistic regression model was created to identify the influence of each item on having a good response and to design a scale (GAIN scale). ROC curve was performed to analyze the ability to predict improvement in disability (MIDAS scale).

Results: 110 patients were included. 65% were considered good responders. Regression model showed headache frequency and intensity influenced 3:2 on having good response. 10-point weighted scale was designed ascribing 3 points to a $\geq$50% improvement in headache frequency or intensity, 2 points to a $\geq$50% improvement in attack duration or analgesic use, and 1 point if $<$50% improvement was observed. Higher scores in the GAIN scale were very well correlated with improvement in MIDAS scale (predictive capability 91,3%). ROC curve determined 2 best cut-off points classifying patients into 3 groups. MIDAS improvement was presented in 98.1% of patients with $\geq$6 points, 73.7% with 3–5 points and only 26.7% with $\leq$2 points.

Conclusions: Headache frequency and intensity influence equally on Botox® response. The GAIN scale is well correlated with improvement in disability. It is a quicker and easier method that could be used as an assessment measure for other migraine preventative treatments.

PO096

Migraine preventive therapy

Onabotulinumtoxina in chronic migraine after one year. Data considering medication overuse and concurrent preventatives in 62 patients

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Background: Long-term response to OnabotulinumtoxinA (OnabotA) in Chronic Migraine (CM) is being confirmed in large series. In real clinical setting CM patients with acute Medication Overuse (MO) or receiving oral preventatives are treated with OnabotA.

Aim: To assess evolution of CM after one year on OnabotA with special focus on MO and concurrent preventive therapy.

Methods: In three Headache Units, data regarding CM patients on OnabotA who had received at least four procedures according to PREEMPT protocol were retrospectively collected. We did not exclude patients with MO nor receiving any preventative at inclusion. OnabotA treatment was continued when at least 30% of reduction in headache days was achieved.

Results: 62 patients (54 females, 8 males) were included. Mean age at first procedure was 39 ± 10.6 years (15–66) and latency between CM onset and OnabotA therapy was 49.8 ± 42.3 months (3–216). They received 7 ± 2.1 treatments (4–13). At inclusion 45 patients (72.6%) fulfilled MO criteria and 56 (90.3%) received a concurrent oral preventive therapy. In 8 cases (12.9%) OnabotA injection was delayed to the fourth month and in 4 (6.5%) temporally stopped. 43 patients (69.4%) remitted to episodic migraine. In 25 out of 56 (44.6%) cases oral preventatives were retired and in 8 (14.2%) a dose reduction was achieved. In 33 out of 45 (63.3%) MO was discontinued.

Conclusion: According to our series, discontinuation of acute medication overuse and oral preventive therapy might be considered realistic goals in real-life long-term using of OnabotA in CM patients.

PO097

Migraine preventive therapy

Migreins and meningioma

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Case report: A 48 aged female was admitted to the hospital at the ED due to a severe headache lasting for about 5 h. None of the taken painkillers provided any help. At the admission the patient mentioned that she has been suffering from migraine headaches for the last 9 years. She reported photophobia and severe eye pain.

At the hospital, the patient received painkillers intravenously, after which she was released home. The next evening, the patient reported back to another hospital with headache, nausea, vomits and problem with the movement. This time, at the admission, all the necessary laboratory, imaging and specialized examinations were performed. In the laboratory examination, ↑CRP, OB and WBC were observed. In ophthalmological examination, problem with vision acuity was diagnosed, Visus, Tonus ER and EL were slightly elevated. In the fundus examination papilloedema was demonstrated. In the neurological examination, a decrease of left side muscle strength was diagnosed. In the head MR, a hypointense tumor with dimensions of 33x30mm was detected, evidencing meningioma presence in the right occipital area. The patient underwent a surgical intervention to remove the tumor.

Earlier, the patient was complaining for more than one year of migraine headaches, which occurred more frequently than once a month (ca. every 10 days lasting each time about 4–5 days). Despite the taken medications, she still complained of photophobia and headaches. Migraine attacks were linked with stress and demanding boss.

Conclusions: Not every migraine attack result only from migraine or stress, but it may be the first symptom of a brain tumor.

PO098

Migraine preventive therapy

Occipital nerve stimulation for drug-resistant chronic migraine: long term efficacy

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Introduction: Although some prophylactic medications have been proposed to treat chronic migraine (CM) there are still many refractory patients and other treatments are warranted. Peripheral nerve stimulation (PNS) of the occipital nerves is a potentially promising therapy for CM patients.

The aim of this study is to evaluate the long-term efficacy and tolerability of PNS of the occipital nerves for the treatment of refractory CM.

Material and Methods: Twenty three patients (10 men, 13 women, average age 51.4 ± 12.1) meeting the IHS criteria for refractory CM were enrolled in this study and implanted with a neurostimulation device near the occipital nerves. The primary endpoint was the reduction in Analogical Visual Scale (AVS). Patient satisfaction, migraine frequency, side effects and reasons for discontinuation were also studied. The follow-up period was 3.1 years.

Results: Headache severity according to the AVS was reduced from 8.9 ± 0.7 before PNS to 3.6 ± 2.7 after treatment initiation. There was also a significant difference in reduction of number of headache days and 80% of the patients were satisfied or very satisfied with the procedure. The most common adverse event was persistent implant site pain and only one patient required to be explanted due to inefficacy.

Discusion: PNS has been explored as a possible treatment option in selective drug-resistant primary headache disorders and, according to our results, this technique may be effective, safe and well tolerated in treating refractory chronic migraine in the long term. An increasing experience and a more routine use of PNS can be forecasted in the future.

PO099

Migraine preventive therapy

Transcranial direct current stimulation: preliminary data in drug resistant migrainous patients

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Background: abnormal excitability of cortical areas may represent a pivotal role in migraine pathophysiology. Transcranial direct current stimulation (tDCS) is a non-invasive and safe technique that modulate the activity of the underlying cerebral cortex. The efficacy of this treatment is still controversial due to the different setting procedure (electrode location, frequency/intensity of stimulation etc.).

Aim: exploring the potentiality of different tDCS setting in treating migraine, evaluating the efficacy of cathodal tDCS, ipsilateral to the frontal hypothermia detected by thermography, as preventive add-on treatment in chronic migraine.

Method: 60 patients with chronic migraine (20 M and 40 F, with a mean age of 45 ± 3.7 years) were randomized to receive 5 consecutive and 2 "recall" sessions, one month apart, of active/sham tDCS for 10 minutes (1.5 mA). The site of application of the electrodes was determined under thermographic guide (hypothermic patch) by thermocamera i3/i5/i7 FLIR. All subjects were treated with topiramate 50 mg bid. Attack frequency and duration, severity of pain and number of headache days were recorded 1 month before, and at 3 months follow-up.

Results: In our experience only a preventive treatment with cathodal tDCS showed a gradual reduction up to disappearance of the cold patch in all patients. A parallel reduction of attack frequency, headache days, attack duration and symptomatic medication intake was noticed; the clinical improvement lasted until the 3-month follow-up.

Conclusion: our results suggest that the application of cathodal tDCS over the frontal hypothermic patch region might be an effective prophylactic therapy in migraine patients.

PO100

Migraine preventive therapy

Three years of experiences with onabotulinumtoxin a in patients with chronic migraine in Czech republic

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Objective: To assess efficacy, safety and tolerability of onabotulinumtoxin A as headache prophylaxis in adults with chronic migraine in Czech Republic.

Background: Several studies have demonstrated a effect of onabotulinumtoxin A in patient with refractory chronic migraine.

Design/methods: Diagnosis was made by ICHD-III criteria for chronic migraine. MIDAS and HIT-6 was applied in all patients at week 0 and at follow-up, and every three months after first injection. Patients diary was provided for six months for documentation of headache episode frequency. All patients had poor headache control, poor quality of life, high disability scores and high acute medication intake. Subjects were treated to injections every 12 weeks of onabotulinumtoxin A (155 U). The primary endpoint was mean change from baseline in headache episode frequency at week 24. The second endpoint was mean change from baseline in HIT-6 and MIDAS at week 24.

Results: We reported data of 26 patients mean age 48 years (median 47 years), who fulfilled ICHD-III beta criteria for chronic migraine Mean score on a pain scale of

0–10 were 8 (standard deviation 2) at week 0, MIDAS grade IV (severe disability) at week 0 and HIT -6 mean score 62 (median 62) at week 0. Fourteen patients interrupted treatment for lack of efficiency at week 12. The subjects had not any adverse event.

Conclusions/Relevance: About fifty percent of our patients had the effect of treatment with onabotulinumtoxin A.

PO101

Migraine preventive therapy

Relationship between induced cognitive and affective qualities of sensation and clinical effects of occipital nerve stimulation in the treatment of chronic migraine

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Background: Occipital Nerve stimulation (ONS) induces sensory experiences in the distribution area of occipital nerves and can be used for treating chronic migraine. The aim of this therapy is to activate antinociceptive mechanisms for preventing migraine. The relationship between cognitive and affective properties of the induced-sensations and the clinical efficacy in the treatment of migraine is unknown.

Aim: To evaluate the relationship between characteristics of sensations induced by ONS and clinical treatment effects.

Methods: 31 patients treated by ONS, were included in our study in the time period from November 2011 to January 2015. We used a new computer-based imaging method (Göbel et al., Brain Stimulation 2015;8(2):295–8) for mapping the spatial, cognitive and affective sensory effects of ONS. We analyzed 808 individual quantitative and qualitative data sets of the relationship between sensory and clinicalstimulation effects.

Results: There is a highly significant effect between properties of sensation and theclinical effects of ONS. Sensations described as tingling, humming and vibrating-show a highly significant greater effect than sensations described as pinching, knocking and pulsating. The group of patients classifying these sensations asunpleasant, demonstrates a higher clinical efficacy than the group of patientsclassifying these as pleasant.

Conclusion: The induction of specific sensation characteristics through ONS is an important predictor for clinical treatment results. Initial and later programming during the course of ONS therapy can significantly improve the therapeutic modulation of antinociceptive systems through targeted elicitation of cognitive and affective sensation patterns.

PO102

Migraine preventive therapy

A study on the long-term use of flunarizine in migraine prevention

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Background: Flunarizine is an effective and widely used preventative for migraine. However, it is not licensed by the United States Food and Drug Administration nor the United Kingdom Medicines Healthcare Products Regulatory Agency. The long term efficiency and tolerability of flunarizine for migraine is not clear.

Aim: We looked at the long term use of flunarizine in patients with migraine-including those with long term use of more than 24 months.

Method: This was a retrospective study conducted at the National Hospital for Neurology and Neurosurgery. Patients followed up since 2010 with prior flunarizine use were identified. Patients with previous, but not ongoing use, and patients with a single prescription at initiation only were excluded.

Results: Ninety-one patients were prescribed flunarizine between 1 January 2010 and 31 December 2013. At maximum tolerated dose, 34% of patients sustained flunarizine for up to 6 months, 37% more than 6 but less than 24 months and, 29% more than 24 months, the longest 16 years and ongoing. The most common adverse effects were depression (35%), weight gain (16%), sedation (14%) and extrapyramidal features (8%). Lack of efficacy,

depression and weight gain were the most common reasons for discontinuation, accounting for 53%, 44% and 15% respectively.

Conclusion: Flunarizine can be an effective and tolerated preventative for long term use in migraine. The most common adverse effect is depression.

PO103

Migraine preventive therapy

Vestibular migraine and persistent postural-perceptual dizziness: results of a double blind, parallel group, pharmacologic dissection trial using verapamil and sertraline

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Background: In 2012, the International Headache Society and Barany Society jointly defined vestibular migraine (VM) and probable VM (pVM). Many patients with VM have chronic vestibular symptoms, which may reflect chronic mechanisms of VM or comorbid disorders such as persistent postural-perceptual dizziness (PPPD). PPPD is the ICD-11 draft term for the condition known as chronic subjective dizziness or phobic postural vertigo. It is reported in 30% of patients with VM, and like VM, has no diagnostic biomarker. Thus proper diagnosis of patients with episodic and chronic vestibular symptoms and headache is uncertain.

Aim: To investigate diagnostic margins of VM.

Method: We used pharmacologic dissection, a technique in which differential effects of pharmacologic probes segregate mixed syndromes. Verapamil, a migraine prophylactic with no known effect on PPPD, was compared to sertraline, a PPPD treatment with little benefit for migraine. 32 patients with episodic and chronic vestibular symptoms and headache meeting criteria for VM plus PPPD were randomly assigned to 12 weeks of double blind treatment with verapamil or sertraline.

Results: Ten patients completed the trial in each arm (19/20 with pVM). Four withdrew for medication intolerance. Eight were excluded for confounds (mostly moderate anxiety or depression) per strict pharmacologic dissection methodology. Final modal doses were verapamil 240 mg/d and sertraline 100 mg/d. Sertraline outperformed verapamil on headache frequency/severity and disability from headache and dizziness ($p < 0.05$).

Conclusion: These results support a narrow definition of VM. Different pathophysiologic processes may underlie chronic dizziness and weaker associations of migraine and vestibular symptoms in pVM.

PO104

Migraine preventive therapy

The use of butulinium toxin type a (BoNTA) injection in treatment of chronic migraine in pediatric practice

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Introduction: Migraine in children occurs in approximately 6 percent of children and affects school work, extracurricular activities and quality of life. Chronic migraine (>15 headache days per month) is particularly devastating. Although botulinum toxin Type A (BoNTA) has been proven effective for treating chronic migraine in adults, little literature exists about its use in children. Here, we present the clinical characteristics and treatment response in children with chronic migraines treated with BoNTA at our institution.

Method: Retrospective analysis of 25 adolescent migraineurs who met IHS III-b criteria for chronic migraine and were treated with BoNTA injection according to the standardized adult protocol. Descriptive statistics and paired t-tests were performed.

Results: Participants ($n = 25$) were 16.7 ± 1.34 years old and 80% female. All had failed standard pharmacotherapy including amitriptyline and topiramate. An average of 2.5 ± 1.7 number of BoNTA injection cycles were performed. Migraine severity decreased significantly from 7.3 ± 1.35 on a 10 point scale to 4.76 ± 2.9 ($p < .001$) and headache frequency from 24.5 ± 7.68 painful days per month to 14.4 ± 12.3 painful days per month ($p < .001$). 1 patient developed nausea related to injection; all others tolerated it well with no side effects.

Conclusion: BoNTA injection was a safe and effective therapy for chronic migraine in our cohort of children recalcitrant to medical therapy. Further research is warranted to evaluate for the long term safety and efficacy in this population.

PO105

Tension type headache

Effectiveness of manual therapy for the management of cervicogenic headache: a meta-analysis of randomized trials

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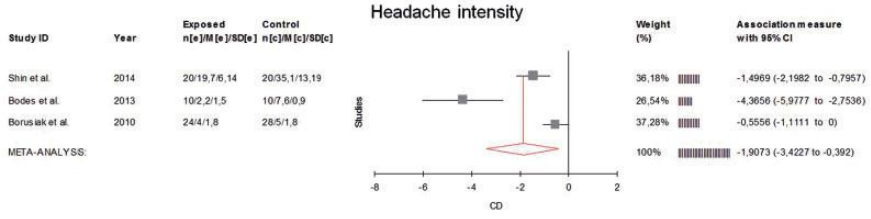
Background: Manual therapy is one of the most commonly used treatment modalities for the management of cervicogenic (CeH).

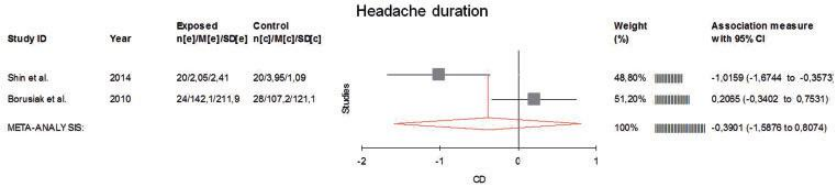
Aim: To determine the efficacy of manual therapy vs. placebo for the management of CeH patients by conducting a meta-analysis of randomized controlled trials (RCT).

Methods: PubMed, MEDLINE, EMBASE, AMED, CINAHL, EBSCO, Cochrane Database of Systematic Reviews, Cochrane Collaboration Trials Register, PEDro, and SCOPUS were searched from their inception through December 2014 All RCT comparing any kind of manual therapy vs. placebo for treating CeH were included. Data were extracted and methodological quality assessed independently by 2 reviewers. We pooled headache intensity and duration as outcomes. The weighted mean difference (WMD) between manual therapy and placebo was used to determine effect sizes.

Results: Three randomized controlled trials met our inclusion criteria and were included in the analysis. Two different therapies were investigated: spinal manipulation or trigger point therapy. Quality of RCT was moderate (mean: 6/10 points). Pooled analyses suggested that manual therapy was more effective than placebo in reducing headache intensity (WMD −1.9073 95%CI −3.4227 to −0.392, Figure 1), but not in reducing headache duration (WMD −0.3901 95%CI −1.5876 to 0.8074, Figure 2) immediate after treatment.

Conclusions: Few RCT investigating manual therapies against placebo for the management of CeH have been conducted. Manual therapy seems to be effective for reducing headache intensity at short term in individuals with CeH. The effectiveness for reducing headache duration was inconclusive. Future high-quality RCTs are needed to further determine the effects of manual therapies in CeH.





PO106

Tension type headache

The number of active trigger points is associated with disability and anxiety in tension type headache

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Background: Previous studies showed that the referred pain elicited by active trigger points (TrPs) reproduces the pain pattern in tension type headache (TTH). However, we do not know if active TrPs are associated to disability and psychological factors.

Aim: To investigate the association between the presence of active TrP with headache-related disability, depression and anxiety in TTH.

Methods: Women with TTH diagnosed by experienced neurologists according to International Headache Classification (ICHD-III) were included. Exclusion criteria included other primary headache, medication overuse headache, whiplash or fibromyalgia. TrPs were bilaterally explored within the masseter, temporalis, upper trapezius, sternocleidomastoid, splenius capitis, and suboccipital. Headache pain-related disability was assessed with the Headache Disability Inventory (HDI – emotional and physical subscales). The Hospital Anxiety and Depression Scale (HADS) and State-Trait Anxiety Inventory (STAI) were used to assess depression and anxiety. Pearson's correlation coefficients were used to determine correlations between the number of active TrPs, HDI, HADS and STAI.

Results: Fifty women (age: 49, SD: 11) with a frequency of 16 days/month (SD: 8) participated. Each women with TTH exhibited 3.7 ± 2.2 active TrPs. The number of active TrPs was positive and moderate associated with the physical subscale of the HDI (r: 0.308; $P = 0.037$) and STAI trait (r: 0.310; $P = 0.036$): the higher the number of active TrPs, the higher the physical disability or the more anxious trait.

Conclusion: The number of active TrPs was associated with headache disability and anxiety trait in a cohort of women with frequent episodic or chronic TTH.

PO107

Tension type headache

Yokukannsannka-chinpihange(chinese herbal medicine) as the treatment for tension-type headache

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Yokukannsannka-Chinpihange is a commerciallyavailable Chinese herbal medicine. This drug consists of three ingredients;Yokukannsan decreases muscle tension and inflammation, and is effective totreat neurosis, hypersensitivity, insomnia and convulsions, Chingi and Hangeare effective to control neurosis, nausea and appetite. Yokukannsannka-Chinpihange is clinically indicated for neurosis and insomniaunder the Japanese health insurance program. Based on its effects, thismedicine should theoretically be effective for patients with irritabletension-type headache. However, no previous studies have reported the clinicaleffects of Yokukannsannka-Chinpihange for the patients with tension-typeheadache. We therefore investigated the clinical effects of Yokukannsannka-Chinpihangefor tension-type headache.

Thediagnosis of a tension-type headache was made in the outpatient clinic at ourhospital. All clinical diagnoses were determined by a single headachespecialist (the author). Yokukannsannka-Chinpihange was given to selected adult-patients diagnosed to have a tension-type headache, especially a headacheassociated with an irritable/neurotic personality. Yokukannsannka-Chinpihangewas prescribed for the patients at a dose of 3.7 grams, twice per day (beforebreakfast and dinner). The clinical effects were evaluated by the patientsthemselves using a visual analog scale and the short form 36 questionnaire morethan one month after starting treatment with the medication.

A total of 26 patients participated in this study. Mostof the patients were able to take the medication regularly. The final outcomewas very effective in 13 patients, effective in eight patients and no effect inthree patients. Based on our results, Yokukannsannka-Chinpihange is effectivefor most patients with tension-type headaches.

PO108

Tension type headache

Correlation between tension type headache and various forms of nociceptive and neuropathic orofacial pain

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Background: Orofacialpain (OP) is a common problem touching 17–26 % of general population. It shouldbe stressed, that both nociceptive and neuropathic pains must be taken intoaccount. Tension typeheadache (TTH) is a very frequent disease with a lifetime prevalence of over80%. There is evidence, that TTH mayremain in relation with muscular pain emanating from pericranial/masticatorymuscles.

Aim: The aim ofthe study is the assessment of the relationship between tension type headacheand various forms of nociceptive and neuropathic orofacial pain.

Method: Patientsaged between 19 and 78 years (n = 412) seeking treatment due to their OP problemswere included into the research. The diagnostic process consisted of thoroughanamnestic examination in line with guidelines of IHS and IASP and functionalexamination proposed by EACD and AAOP. All subjects were examinedradiologically. Patients were divided into four groups and ascribed to themdepending on the presence of pain: isolated nociceptive muscular, nociceptivemuscular and articular, nociceptivemuscular with concomitant continuous neuropathic, isolated neuropathic pain. Acorrelation between different kinds of orofacial pain and the presence of TTHwas analyzed.

Results: There was aclear positive relationship between nociceptive pain in the trigeminal systemand TTH. No significant correlation between isolated continuous neuropathic and TTH could be stated.

Conclusions: The resultsof the study may support the potential relationship between TTH andnociceptive muscular pain ofpericranial/masticatory structures. The link between neuropathic pain and TTHremains unclear and requires further research.

PO109

Tension type headache

Association between the Val158met polymorphism and the number of active trigger points in children with tension type headache: a pilot study

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Background: Previous studies found an association between Val158Met polymorphism and pressure pain sensitivity in children with tension type headache (TTH). In addition, the referred pain elicited by active trigger points (TrPs) reproduces the pain pattern in children exhibiting TTH.

Aim: To investigate the association between the Val158Met polymorphism and the number of active TrP in children with TTH.

Methods: Children with TTH diagnosed by an experienced neuropediatrist participated. Exclusion criteria included other primary or secondary headaches, medication overuse headache, and any comorbid medical condition. TrPs were bilaterally explored in the temporalis, masseter, superior oblique, upper trapezius, sternocleidomastoid, suboccipital, and levator scapulae muscles. After amplifying Val158Met polymorphism by polymerase chain reactions, we determined genotype frequencies distributions. We classified children according to their Val158Met polymorphism: Val/Val, Val/Met, or Met/Met. A 1-way analysis of variance (ANOVA) was used to determine differences in the number of active TrPs among the genotypes.

Results: Forty-four children (75% girls, age: 9, SD: 2 years) with a frequency of 13 days/month (SD: 2) participated. Each children with TTH exhibited 4.0 ± 1.7 active TrPs. Children with Met/Met genotype showed a greater number of active TrPs (mean: 6 ± 1) than children with Val/Met (mean: 3.7 ± 1.5) or Val/Val (mean: 4 ± 1) genotype ($F = 4.007$; $P = 0.026$).

Conclusion: The presence of the Met allele of the Val158Met polymorphism was associated with more number of active TrPs in children with frequent episodic TTH. However, due to the small sample size, future studies are now needed to further confirm this association.

PO110

Tension type headache

The number of active trigger points is negatively associated with restricted cervical range of motion in children with tension type headache

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Background: Current evidence shows that children with tension type headache (TTH) exhibit musculoskeletal disorders of the cervical spine including trigger points (TrPs) and restricted cervical range of motion (CROM). No study investigated the association of active TrPs with CROM.

Aim: To investigate the association between the number of active TrPs and active CROM in children presenting TTH.

Methods: Children with TTH diagnosed by experienced neuropediatrist participated. Exclusion criteria included other primary and secondary headaches, medication overuse headache, and any medical condition. TrPs were bilaterally explored in the temporalis, masseter, superior oblique, upper trapezius, sternocleidomastoid, suboccipital, and levator scapulae muscles. Active CROM in flexion, extension, both lateral-flexion and both rotation was also assessed. Spearman correlation coefficients were calculated to determine correlations between the number of active TrPs and cervical range of motion.

Results: Fifty-two children (70% girls, age: 9, SD: 3 years) with a frequency of 12 days/month (SD: 2) participated. Each children with TTH exhibited 4.0 ± 1 active TrPs. The number of active TrPs exhibited negative associations with CROM in both lateral-flexion (left: r_s: -0.287; $P = 0.039$; right: r_s: -0.248; $P = 0.045$) and rotations (left: r_s: -0.350; $P = 0.011$; right: r_s: -0.397; $P = 0.004$), but not with cervical flexion or extension ($P > 0.4$): the higher the number of active TrPs, the lesser the bilateral CROM in lateral-flexion and rotation.

Conclusion: We found that the more TrPs, the more limitation in CROM in children with frequent episodic TTH. It is possible that proper TrP management has a therapeutic effect in CROM.

PO111

Tension type headache

Control/cure naturally the headache/migraine just by touching the tips of your fingers

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[1]*Acupuncture, Sujok Association of India, Delhi, India*

Sujok Is A Natural Way Of Healing Without Any Drugs or Side Effects.

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"Sujok" Is A Korean Therapy Developed By Late Prof. Park Jae Woo, A Korean Scientist Approx. 41 Years Back.

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SuJok Acupuncture is a Physical & Metaphysical, Natural Therapy of healing without drugs.

It is an instant and effective healing therapy without medication and is absolutely safe and does not have any side effects.

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Stressed and depressed? The newest health funda in town gives you tips to rejuvenate in a quick and easy-to-learn manner.

NEW THERAPY

Times of stress? Marital and other mess? We suggest don't panic. Just er... press...your fingers the Sujok way and heal yourself. So says Dr Pradeep Sharma, a pioneering healer of Sujok (a Korean art developed in Russia). His clinic at GK-1 looks like a shrunk globe with an Australian student, Siberian herbs, Hindu chants and the photo of the Korean master - Park Jae Woo.

Sujok what?

Well, Sujok's a derivative of the traditional acupuncture and pressure systems, but Woo made it more scientific. In the traditional system, the points on the hand do not correspond to the body, and that's what Sujok innovates upon. In Sujok, the thumb stands for the head, the other four fingers are two limbs each. The entire body, says Sharma, can be healed by pressing just one finger.

Sujok sensei

Sharma is on a teaching spree as well for he wants a Sujok doctor in every home. He charges a modest 5,500, all equipments included, and teaches in 24 working hours flat. And he heals you in 16 sessions if you have a chronic ailment.

Here are a few tips from the guru:

Stressed?

The tip of each finger corresponds to the brain. Touch the tip of the first finger with your thumb. That's the yogi pose. It'll induce calm, cure headaches.

Insomniac?

Apply dark blue colour with a marker, in half circles, on tips of fingers and join the fingers of the two hands. Do this for 4 days and see the difference. Don't do it in your office. You might lose your job snoring!

Problems in the couch?

"The root of sex and sensuality is the brain," says Sharma, so join the tips of fingers of both hands. Relax first. At the somatic, bodily level, the lower edge of a finger corresponds with the genitals (can you beat that!). Press the edges of the fingers with a pencil. The pressure applied on the fingers sends magnetic waves to the brain. These waves heal and detoxify. So relax and get Sujoking!

Sujok Clinic, B-231, LGF, GK-1. Call: 51431440

Sujok basics

Sujok , a Korean therapy cures disease by stimulation of the hands and feet with combined use of acupuncture and acupressure aids. In Korean 'Su' means hands and 'Jok' means feet.

Endowed with exquisite remote control function,our hands and feet can cure diseases throughout the body.

Developed by Prof. Park Jae Woo 30 years back, it is a phsical and metaphysical, natural therapy of healing without drugs.

The treatment is carried out using micro needles, micro magnets, micro and mini moxa, rollers, ring massagers, inserters, seeds and herbs.

AMIT RANJAN

1. Sress-buster 2. Sleep-inducer. 3. The sensual prick.

PO112

Tension type headache

Specific strength training for adult tension-type headache patients. A randomized, controlled study

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Background: Specific Strength training has shown effect in reducing musculoskeletal pain in the neck. As neck pain is highly prevalent in Tension-type Headache (TTH) patients, it is relevant to also examine the effect of specific strength training of the upper shoulder muscles on TTH patients.

Aim: To examine the effect of specific strength training of the upper shoulder muscles on TTH frequency and duration.

Methods: 60 TTH patients were included after completing one month headache diary, to ensure they fulfilled the (ICHD2) criteria for TTH, and had TTH $\geq$8 days per month. TTH patients were randomized into training and a control group. The specific strength training group trained upper shoulder muscles 10 weeks with rubber bands. The control group was instructed in ergonomics and posture correction. During the 10 week intervention period, and 12 weeks follow up frequency, and duration of headache were recorded in a diary. Mean values and SD are presented.

Results: 23 patients completed strength training, and 21 completed the control group. Specific strength training resulted in significantly lower headache duration (hours) at follow-up ($p = 0.036$) 227 (166) compared to baseline 252 (153). Significantly lower frequency at follow-up (days) ($p = 0.047$) 17 (10) compared to baseline 19 (9). Control group had also significantly lower headache duration at follow-up ($p = 0.041$), 144 (117) compared to baseline 198 (138), and frequency was lower at follow-up ($p = 0.0033$) 13 (7) compared to baseline 17 (7).

Conclusion: This randomized controlled trial showed significant lower TTH duration and frequency after both strength training of upper shoulder muscles, and by the ergonomics and posture control intervention.

PO113

Tension type headache

A double blind randomized placebo controlled trial for non-invasive dynamic trans-cutaneous electrical nerves stimulation in management of tension type headaches: the first results

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Background: We presented the design of this study last year [1]. Here are the first results we got.

Objectives: To compare Dynamic transcutaneous electrical nerves stimulation (DENS) and placebo for pain relief in patients of different age suffering from frequent (10 day/month) or chronic tension type headaches.

Methods: We have 39 patients in each group now, this gives us the power 0.8 allowing to make the first preliminary statistical analysis. The data involve four subjective reports of pain (scored from 0 to 10) per patient for 10 day of observation: morning, just before procedure, just after procedure, and evening. Three different effects were analyzed: Short-time (comparing headache scores before and after therapy); medium-time (comparing scores in the morning and in the evenings of the same day); long-time effect (comparing the changes in headache scores during the 10 days course).

Results: When we analyzed the data across all age group, there was no significant difference between DENS and placebo. Subgroup analysis showed significant medium term effect in the elderly (mean age 58.5) – DENS was better with $p = 0.015$. In patients of 25 years and younger, DENS became significantly better in alleviating morning headache, $p = 0.037$. For short-time effect DENS was better with $p = 0.067$ for the adolescents (mean age 14.8).

Reference

1. Akhmadeeva L., Valeeva D., Naprienko M., Goldobina L., Rayanova G. and Veytsman B.. A double blind randomized placebo controlled trial for non-invasive dynamic trans-cutaneous electrical nerves stimulation in management of tension type headaches. *The Journal of Headache and Pain* 2014; 15(Suppl 1): P.89.

PO114

Tension type headache

Thermal sensitivity by migraine phase: a blinded longitudinal study

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Background: Several studies suggest that pain thresholds are lower in migraineurs between attacks compared to headache-free controls and that thresholds decrease further before, during and after a migraine attack.

Aim: To explore the cyclic nature of migraine by measures of thermal pain and to compare the measures to controls in a blinded longitudinal study.

Methods: Fourty-nine migraineurs were examined four times and 31 controls once with thenar and frontal cold (CPT) and heat pain thresholds (HPT). Headache diaries classified examinations as interictal, preictal, ictal or postictal with a one-day limit. Intraindividual thresholds were analyzed with linear mixed models (LMM) with pain threshold as the dependent variable, migraine phase as fixed factor and subject as random factor. Pain thresholds of interictal recordings from 45 migraineurs and 31 controls were compared using Mann-Whitney U Test. Pain threshold definitions: $CPTd = 32^{\circ}C - CPT$ and $HPTd = HPT - 32^{\circ}C$.

Results: Frontal CPTd were decreased ictally (LMM mean change -1.99 [95% CI -3.80, -0.32] $^{\circ}C$, $p = 0.019$).

Thenar CPTd were lower in interictal migraineurs compared to controls (mean $\pm$ SD $20.0 \pm 6.0^{\circ}C$ vs. $22.6 \pm 5.3^{\circ}C$, $p = .022$).

Preictal changes were not seen.

Conclusion: Ictal forehead cold suballodynia, and lower interictal thenar CPTd compared to controls, are in concordance with previous studies, but preictal suballodynia was not confirmed. Cold allodynia may accordingly be a thermal pain feature that reflects a slight generalized hypersensitivity in migraineurs.

PO115

Tension type headache

The effectiveness of CoQ10 in the treatment of tension headache

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Objective: The objective of the study is to evaluate the effectiveness of CoQ10 in the treatment of tension headache.

Background: Tension headache is generally a diffuse, mild to moderate pain in the head that is often described as a tight band-like feeling around the head. A tension headache (tension-type headache) is the most common type of headache, yet its causes are not well understood. Managing a tension headache is frequently a balance between encouraging healthy habits, finding effective non-drug treatments and using medications properly.

Methods: 200 patients were evaluated according to IHS classification of headaches at the Pain & Headache Center, IMC, KSA. Patients were randomly allocated to either CoQ10 200 mg, daily, alone, or in combination with Tizanidine or Amitriptyline, at bedtime. Both groups were allowed to have an average of 10 sessions of Physical Therapy. First group (N = 110) received CoQ10 200 mg, once daily, and Tizanidine 2 mg, or Amitriptyline 5 mg, at bedtime. While the second group (N = 90) received Tizanidine 2 mg or Amitriptyline 5 mg only. Inclusive criteria: 80 males, 120 females; ages between 25–65 years, with a mean of 45. Exclusive criteria: pediatrics, patients older than 55, with uncontrolled diabetes and blood pressure, and other neurological deficits.

Results: Average improvement of 80% and 60% were seen in patients who were treated with the combination therapy (CoQ10 and Tizanidine or Amitriptyline), and Tizanidine or Amitriptyline alone, respectively.

Conclusion: Patients receiving the combination therapy of CoQ10 and Tizanidine showed more significant symptomatic improvement compared to those receiving Tizanidine or Amitriptyline alone.

PO116

Cluster headache and other trigeminal autonomic cephalalgias

Refractory chronic cluster headache: a consensus statetment on clinical definition from the european headache federation

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Background & Aim: Chronic cluster headache (CCH) often resists to prophylactic pharmaceutical treatments resulting in patients' life damage. In this rare but pragmatic situation escalation to invasive management is needed but framing criteria are lacking. We aimed to reach a consensus for refractory CCH definition for clinical and research use.

Methods: The preparation of the final consensus followed three stages. Internal between authors, a larger between all European Headache Federation members and finally an international one among all investigators that have published clinical studies on cluster headache the last five years. Eighty-five investigators reached by email. Proposed criteria were in the format of the International Classification of Headache Disorders III-beta (description, criteria, notes, comments and references).

Results: Following this evaluation eight drafts were prepared before the final. Twenty-four (28.2%) international investigators commented during two rounds. Refractory CCH is described in the present consensus as a situation that fulfills the criteria of ICHD-3 beta for CCH with at

least three severe attacks per week despite at least three consecutive trials of adequate preventive treatments. The condition is rare, but difficult to manage and invasive treatments may be needed. The consensus addresses five specific clinical and paraclinical diagnostic criteria followed by three notes and specific comments.

Conclusion: Although refractory CCH may be not a separate identity these specific diagnostic criteria should help clinicians and investigators to improve patient's quality of life.

PO117

Cluster headache and other trigeminal autonomic cephalalgias

Cluster headache responding to indomethacin

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Background: Cluster Headache (CH) attacks respond to 6 mgsubcutaneous sumatriptan and/or to inhaled oxygen. These treatments areeffective in over 80% of cases. Aim Anectodalevidence suggests that some CH patients may respond to indomethacin, as doabsolutely patients with paroxysmal hemicrania and hemicrania continua. Wereport the case of a man with CH, who responded acutely and prophylacticallyonly to indomethacin.

Method: Following the International Classification of Headache Disorders (ICHD-3 beta)criteria, we diagnosed with CH a 72-year-old male, whose headaches started whenhe was 56. For the first 4 years CH was episodic and later became chronic. Themean frequency of attacks was two per day, and their duration was about 30minutes. MRI of the brain was normal. The attacks never responded tosubcutaneous sumatripan and to oxygen inhalation. Interestingly, the patientnoticed that his attacks could promptly and completely subside by injecting 50 mg intramuscular indomethacin.

Results: Thepatient was previously treated prophylactically with verapamil, prednisone andlithium, reporting no benefit. Given the absolute response to acute parenteralindomethacin, the patient was commenced with preventive oral indomethacin atthe dose of 50 mg, three times a day. He showed a complete response after aweek; reduction of the dose consistently led to headache relapse.

Conclusion: A response to indomethacinis not contrary to ICHD-3 beta criteria for CH. The review of the literaturesuggests that indomethacin-responsive CH exists and that some cases may bemisdiagnosed when one relies on therapeutic responsiveness to make a diagnosis.

PO119

Cluster headache and other trigeminal autonomic cephalalgias

Thalamic dysfunction in spontaneous chronic refractory cluster headache attacks

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Methods: The prospective observation started in May 2012. We investigated cerebral glucose metabolism using [(18)F]-fluorodeoxyglucose (FDG/PET-TC as an index of neural activity, during spontaneous cluster headache (CH) attacks in 6 patients (4 males, 2 females age range 18–52) who suffer from chronic CH (attacks/day = 7–11) refractory to all conventional acute and prophylactic therapies as well to different types of electrical stimulation, e.g. DBS, ONS. A control group including 6 sex, age matched subjects personally and familiarly exempts from any primary pain was provided. Normalized FDG uptake values were calculated with reference to the pons. PET images were analyzed with regions of interest (ROI) and statistical parametric mapping (SPM) approaches. Following the first session, patients have to underwent functional imaging observation every 2 years or till amelioration.

Results: During CH attacks, hypometabolism was seen in the contralateral ventroposterior thalamus. The youngest patients (age 18 and 21 years) evidenced a first result (September 2012, December 2013, respectively) in which hypometabolism was more diffuse in thalamus and also at the level of hippocampus. Above mentioned hypometabolism was seen only in the pain state and was never evidenced in controls.

Discussion and Conclusion: These outcomes enlighten dysfunction of thalamus in the pathophysiology of refractory chronic CH. None of the subject show any substantial clinical change versus first visit except for the 2 mentioned young sufferers who show clear worsening. We propose that refractory CH pain might be linked to functional alteration paralleling a functional diaschisis associated to sprouting in discrete CNS areas.

PO120

Cluster headache and other trigeminal autonomic cephalalgias

EKG control during verapamil use in headache: an international delphi study

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Background: Verapamil is the (off-label) mainstay in prophylactic treatment of cluster headache. To screen for cardiac contraindications electrocardiograms (EKGs) are generally advised during treatment. The treatment guidelines for cluster headache however are limited with respect to EKGs.

Aim: To check for consensus among cardiologists specialized in rhythm disorders on the need for EKG control before and during verapamil treatment for cluster headache.

Method: We used the Delphi approach (two rounds) by including an international panel of 22 cardiologists specialized in the field of cardiac rhythm disorders who were randomly identified from membership list from the Heart Rhythm Society. Consensus was defined if >80% agreed to a proposition.

Results: Eighty-two percent agreed that an EKG should be made prior to the first start of verapamil. Half of respondents recommended to make EKGs during stable doses at set times, especially with mean daily doses of ≥330 mg (mentioned range: ≥120–480 mg).

Half of the panellists advised to make an EKG *before* any increase of the dose of verapamil, and 60% advised an EKG *after* dose increase.

In case of high doses of verapamil (defined as ≥480 mg per day) 50% of panellists advised to do ambulatory EKG holter monitor registration instead of regular EKG.

Conclusion: Consensus was obtained only for one of the six propositions about the EKG regime: to make a baseline EKG before starting verapamil.

PO121

Cluster headache and other trigeminal autonomic cephalalgias

Distribution of the calcitonin gene-related peptide receptors in the sphenopalatine ganglion of the rat

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Background and Aim: It has been reportedthat the sensory nerve fibers containing calcitonin gene-related peptide (CGRP)or substance P originated in the trigeminal ganglion (TG) are distributed inthe sphenopalatine ganglion (SPG), which is one of the parasympathetic cranialganglia. Recently, the structure of the CGRP receptor has been clarified, andthis makes it possible to explore the localization of the CGRP receptor usingimmunohistochemical technique. In this study, we examined the distribution ofthe CGRP receptor and its spatial relationship with CGRP containing nerve fibersin SPG of rats.

Methods: Sprague-Dawley rats (250–300 g)were used. Afterperfusion fixation, SPGs were dissected and tissue sections (7 μm thickness) were prepared. Immunostaining was performed usinganti-vasoactiveintestinal peptide (VIP), anti-CGRP, anti- receptor activity-modifying protein 1 (RAMP1) and anti- C-type lectin receptor(CLR) antibodies. For quantification, we counted the numbers of neurons positive for each of themarkers in serial six sections.

Results: RAMP1-IR was observed in59% neurons of SPG (6338 neurons, n = 5; range 47.4 ~ 73.7%), and 84% of theseneurons showed CLR-IR (3721 neurons, n = 5; range 75.4 ~ 92.9%). Most of theseneurons also showed VIP-IR. 15% of neurons with RAMP1-IR had nerve fibers with CGRP-IRin close proximity (4652 neurons, n = 5; range 12.4 ~ 21.4%).

Conclusion: The present studyrevealed the possible functional interaction between SPG and TG via CGRPcontaining nerve fibers. These findings may provide an important clue to thepathophysiology of cluster headache.

PO122

Cluster headache and other trigeminal autonomic cephalalgias

Oxygen in cluster headache

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Background: Most cluster headache patients respond to oxygen therapy, but approximately 20–25 % do not.

Aim: The aim of this study was to evaluate the frequency of use of oxygen therapy in our cluster headache patients.

Method: We retrospectively evaluated our cluster headache patients with phone interview. Participants completed a questionnaire with questions about the headache features and the response to oxygen therapy.

Results: A total of 60 patients were included, of whom 46 were men (76.6%), giving a male-to-female ratio of 3:1. Mean current age was 38.2 years (SD 8.8) and mean age at onset of the cluster headache symptoms was 27.2 (SD 0.3). The majority of the participants had episodic cluster headache (96.6%). Mean Numeric Analogue Scale was 9.1 (SD 1.2). Mean number of autonomic features was 3.2 (SD 1.4). Most common autonomic features were lacrimation (n = 42), conjuctival injection (n = 39), eyelid oedema/ptosis (n = 28), forehead and facial sweating (n = 24), rhinorrhoea (n = 21), nasal congestion (n = 19), forehead and facial flushing (n = 11), respectively. Thirty-five patients (58%) went to hospital at least one time for cluster attack within one-year. Twenty-six of all patients (43%) had used oxygen. Nineteen of these patients (73%) thought that oxygen was effective and useful. Twenty-four of all patients (40%) had been offered to buy home-type oxygen tank while only thirteen patients (21%) chose to do so.

Conclusion: Oxygen tank might be used effectively as home therapy for acute treatment of cluster attacks, eventually reducing patients' emergency department visits frequency. Thus this option should be offered to patients.

PO123

Cluster headache and other trigeminal autonomic cephalalgias

Effects of verapamil on ECG in cluster headache patients: a key to underlying pathophysiology?

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Introduction: Cluster headache (CH) is a Trigeminal Autonomic Cephalalgia. Although the hypothalamus appears to be involved in CH pathophysiology, controversies surrounding this remain unsettled.

Verapamil is the prophylactic treatment of choice in CH. However, doses are frequently much higher than those used for other indications. Deciphering why CH patients tolerate high doses of verapamil might help better explain CH pathophysiology.

Method: This is a case series of 13 CH patients on verapamil, dosage from 480–960 mg. ECG was obtained with each 80 mg increment.

Results:

Two patients developed First Degree AV Block; with monitoring and cardiology consultation, medication continued without clinical symptoms. Interestingly, paradoxical shortening of PR interval developed in 6 patients (Table). Bradycardia occurred in 5 patients; none were symptomatic.

Discussion: It is debated whether sympathetic dysfunction or increased parasympathetic tone is the main pathophysiologic feature in CH. Since high doses of verapamil in some CH patients do not cause significant abnormalities in AV node or symptomatic bradycardia, sympathetic dysfunction could occur.

The 'Rostral Ventrolateral Medulla" is a critical structure maintaining blood vessel sympathetic tone.

The pontine 'A5 noradrenergic cell group" has a role in response to hypoxia.

Considering the anatomic orientation of these structures with the hypothalamic Periventricular Nucleus, dysfunction in the tract connecting these structures could explain sympathetic malfunction, response to oxygen in acute attacks, as well as the role of DBS in the posterior hypothalamus in CH treatment.

The precise roles of the brainstem and hypothalamic structures, whether primary or secondary, remains to be determined.

PO124

Cluster headache and other trigeminal autonomic cephalalgias

A case report of sunct syndrome responsive to gliacin

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Background: SUNCT is a rare debilitating primary headache disorder which is characterized by very brief, stabbing pain in the orbital/supraorbital region and ipsilateral conjunctival injection and tearing. Treatment of SUNCT is challenging with no consistent outcomes being reported with any one therapeutic approach. Gliacin™ is a novel, patent-pending derivative of *Boswellia serrata* first shown to have promise for the treatment of various primary headache conditions including trigeminal autonomic cephalalgias.

Aim: Review the case of a patient who has successfully used Gliacin™ for the long term treatment of SUNCT syndrome.

Methods: A single case report of a SUNCT patient successfully treated with Gliacin™ is reported.

Results: A 45 year-old woman experienced the onset of left-sided periorbital pain. The pain was described as "stabbing" and occurred in attacks lasting a few seconds to three minutes (125–150 times per day). Attacks were associated with ipsilateral conjuctival injection, prominent tearing and periorbital edema. Ocular and other secondy etiologies were excluded with exam and diagnostic testing. Ultimately the patient was placed on Gliacin™ and within 72 hours of initiating therapy attack frequency drastically reduced. Attacks dropped from over 100 per day to a few (<5) per month. Attack severity also dropped by 30%. HIT-6 and HQL scores dropped by 38% (78 to 48) and 65% (78 to 27) respectively. The patient reports no side effects or adverse reactions to Gliacin™.

Conclusions: In this reported case, Gliacin™ has been highly effective and well tolerated. Gliacin™ represents a novel herbal preparation that warrants further investigation.

PO125

Cluster headache and other trigeminal autonomic cephalalgias

Neurological effects of piroxicam (pain reliever) may be structure activity based

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The antipsychotic effect of piroxicam (a pain reliever) similar to that of typical antipsychotic and with strong tendency to produce extrapyramidal motor systems may be structurally activity based. Torticollis, opistothonus, and hypotension caused by piroxicam and abated by atropine is suggestive of acetylcholine involvement. This extrapyramidal motor activities may be due to neutral bidentate ligand coordinated to the the metal ion through pyridyl-N and carbamoyl O of the amide moiety, which has

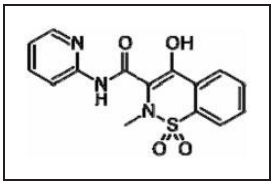

Figure 1. Chemical Structure of Piroxicam

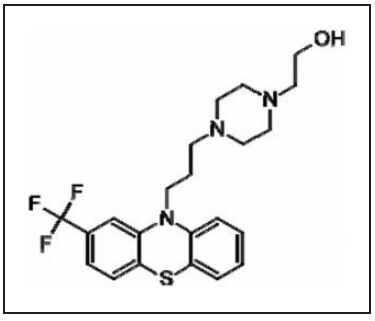

Figure 2. Chemical structure of Fluphenazine

electrostatic effect in protonation/deprotonation equilibria, a marked increase in the activity of the enolic function being caused by pyridinium group, indicating an electron conjugation through the molecule. The penetration of piroxicam through blood-brain barrier (BBB) may be by redox chemical delivery system linking it to the lipophilic dihydropyridine carrier creating a complex with carboxylic acid that transverses the BBB because of its lipophilicity. The complex is enzymatically oxidized to the conic pyridinium salt. Subsequent cleavage of the drug from the pynidinuim carrier leads to sustained drug delivery in the brain parenchyma. Brain uptake of piroxicam may be positively correlated with lipid solubility at high doses or negatively correlated with hydrogen bonding or due to damage to meninges.

Keywords: Piroxicam, typical antipsychotic, cerebellum, structure-activity relationship, enol hydroxide, meninges

PO126

Cluster headache and other trigeminal autonomic cephalalgias

Reduced baroreflex sensitivity in cluster headache patients

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Background: Important elements of cluster headache (CH) pathophysiology may be seated in the posterior hypothalamus. Cranial autonomic features are inherent, but involvement of systemic autonomic control is still debated.

Aim: To characterize autonomic function by investigating baroreflex sensitivity (BRS) in CH patients.

Method: Twenty-six CH patients (in bout) and an equal number of age-, sex- and BMI-matched controls underwent head-up tilt table test. BRS was determined by the sequence method.

Results: Compared to controls, patients exhibited a blunted shortening of RR intervals to falls in systolic blood pressure (SBP) (14.3 vs. 22.3 ms/mmHg, $P < 0.05$) in the supine position. Also, compared to controls, BRS was lower in patients having suffered an attack within the past 12 h (12.5 vs. 22.3 ms/mmHg, $P < 0.01$), opposed to those patients who had not (16.0 ms/mmHg, $P > 0.05$). In the tilted position the drop in SBP at the carotid sinuses was higher in patients who had recently suffered an attack. Despite this they exhibited a less marked shortening of RR intervals when compared to patients who had been attack free for longer.

Conclusion: CH patients exhibit a blunting of BRS which may be affected by the attacks themselves. The fast RR interval fluctuations used in this method reflects cardiovagal responses, thus the blunted responses are suggestive of dysfunction in the parasympathetic division of the autonomic nervous system or in the central relay of impulses from the baroreceptors.

PO127

Cluster headache and other trigeminal autonomic cephalalgias

Aura in cluster headache

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Background: Aura symptoms have been reported in up to 23% of cluster headache patients. In migraine, headache characteristics between patients with and without aura can differ. We do not know if there is a similar difference in cluster headache patients with and without aura.

Aim: In this study we aim to assess (i) the prevalence of aura in cluster headache and (ii) if there is a difference in attack characteristics between cluster headache patients with and without aura.

Methods: In this cross-sectional cohort study aura symptoms before and during cluster headache attacks were investigated, using web-based questionnaires.

Results: Of the 756 subjects who entered our web-based recruitment system, 641 subjects (84.8%) returned all necessary questionnaires. There were 88 patients (13.7%) fulfilling the ICHD-III beta criteria for 'typical aura with headache'. Their aura was characterized by speech/language (59.1%), sensory (38.6%) and visual (27.3%). Cluster headache patients with aura were more often females (40.1% vs 24.6%) and were more often diagnosed with the chronic form of cluster headache (34.1% vs 21.9%). In addition, lacrimation was more often reported

in patients with aura, whereas other attack characteristics were not significantly different.

Conclusion: Aura was reported in 13.7%. of our cluster headache patients, most often involving speech/language. Lacrimation was more often present in patients with an aura compared to those without.

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Cluster headache and other trigeminal autonomic cephalalgias

Paroxysmal hemicrania-tic syndrome as the initial manifestation of multiple sclerosis

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Background: The association of paroxysmal hemicrania with trigeminal neuralgia has been described and was called paroxysmal hemicrania-tic syndrome (PH-tic). We report the case of a patient diagnosed as having PH-tic syndrome as the initial manifestation of multiple sclerosis (MS).

Case report: A forty year old woman was admitted to our hospital suffering from right periocular pain for the last 6 months. The attacks were paroxysmal, neuralgiform, consisting of stroke-like sensations, which developed spontaneously or were triggered by different stimuli in facial and intraoral areas. Parallel with those, she felt a throbbing retro orbital pain with homolateral autonomic symptoms such as conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, and palpebral fissure narrowing. This pain lasted, most often between 10 and 15 min. The bouts were frequent 6–8/day. Beyond hemifacial hypesthesia the neurological finding was normal. MRI study, performed 2 months after the initial symptoms, showed multiple T2-weighted hyperintense lesions, some of them in the right trigeminal main sensory nucleus and root inlet, being hypointense on T1-weighted image. Neurophysiological studies of trigeminal nerve (somatosensory evoked potentials and ephaptic transmission test) correlated with MRI described lesions. The patient's headache bouts have been improved immediately after treatment with indomethacine, and have been completely relieved with lamotrigine, steroids, and beta-interferon for a longer period.

Conclusion: This case might suggest a pathophysiological relationship between the trigeminal main sensory nucleus and PH-tic syndrome. We emphasize here the importance of MRI in people suffering from PH-tic syndrome to assess the final diagnosis, suggestive for MS.

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Cluster headache and other trigeminal autonomic cephalalgias

Cluster headache presentation. Do we know everything?

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Introduction: Despite all descriptions of cluster headache (CH), still little is known about differences in clinical presentation between forms and genders.

Aim: To show CH features in 158 patients, regarding demographics, clinical characteristics, triggers, diagnostic delay and treatment response.

Methods: We performed an observational prospective cross-sectional study. We collected data of all CH patients visiting the specialized headache center in Valencia, Spain for a 7-month period.

Results: *Episodic CH*: n = 100, *chronic CH*: n = 58. *Men*: n = 116, *women*: n = 42. *Pharmacologically treated*: n = 136, *neuromodulation*: n = 22.

Age peak of onset of CH: third decade, women: a second peak – sixth decade. The highest age of onset: primary chronic CH.

Family history: migraine. CH: inherited from father.

Comorbidity: cardiovascular diseases, dyslipidemia, kidney diseases, depression and sleep apnea.

Pain: right-sided, with orbital or periorbital localization. Chronic CH: parieatal and temporal. Women: V1 and V2 pain localization.

Autonomic symptoms: tearing (men: cranial autonomic symptoms, women: migraneous – visual aura.

Headache attack: 30–60'. Number of attacks/24 h: 1–2. Length of cluster period: 1–3 months. Cluster periods/year: 2.

Use of alcohol: men, episodic form.

Smoking: most patients, women: less frequently smokers or ex-smokers than men.

Pharmacological acute treatment: oxygen, sumatriptan. Chronic CH: zolmitriptan i.n., lithium carbonate, indomethacin and blockade of n. occipitalis major.

Prophylaxis – verapimil and topiramate (men: topiramate more often). Drug-resistant chronic CH: ONS and SPG.

CH in women: not related to menstrual cycle.

Diagnosis delay: 5–10 years.

Conclusions: Some differences in CH presentation and therapy response between forms and genders exist. The neuromodulatory methods of treatment show promising results.

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Cluster headache and other trigeminal autonomic cephalalgias

Perceptions, understandings and experiences of cluster headache patients in the north of England: a qualitative study

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Background: Very few qualitative studies on cluster headache have been conducted. As a result we have little in-depth understanding of the perceptions and experiences of cluster headache patients and the health professionals who treat them. With this research we aim to rectify that gap.

Aim: The main objective of the overall project is to gain insight into the perceptions, experiences and understandings of cluster headache from the perspective of three key stakeholder groups: the cluster headache patients, GPs and neurologists. Here, we present the findings of the interview study with cluster headache patients.

Method: A qualitative study using semi-structured interviews with cluster headache patients. A systematic qualitative methodology is applied to the transcribed interviews ($n = 30$). The data are analysed using grounded theory to provide a systematic approach to coding. The following stages of analysis are followed: 1) line-by-line coding; 2) focused coding; 3) axial coding and 4) theoretical coding.

Result: Our findings provide an explanatory framework for patients' views, experiences and understandings of cluster headache. The main themes are: early detection and diagnosis of cluster headache; effective treatment of cluster headache and the management of cluster headache in primary and secondary care.

Conclusion: This research contributes to our understanding of the social context of cluster headache sufferers and it sheds new light on the public and professional responses to cluster headache.

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Cluster headache and other trigeminal autonomic cephalalgias

Does a hyperexcitable cortex link cluster headache, migraine and epilepsy?

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Introduction: Cortical hyperexcitability is hypothesized to be a shared characteristic of migraine and epilepsy with genetic aetiology. The frequent occurrence of aura in cluster headache, and its response to drugs acting on ion channel function may point to cortical hyperexcitability in cluster headache as well. We aimed to investigate the co-occurrence of migraine and epilepsy in cluster headache. When these conditions would prove to be related, this would indicate that cortical hyperexcitability may also be of importance in cluster headache.

Methods: In a large web-based population of cluster headache patients, we investigated cross-sectionally the life-time prevalence of epilepsy and migraine by means of questionnaires.

Results: A total of 12/606 (2.0%) of our cluster headache cohort also had epilepsy, which we classified as idiopathic/probably genetic (0.8%) or structural (1.2%). A total of 70/606 (11.6%) also had migraine. None of our patients had all three conditions (cluster headache, epilepsy and migraine).

Conclusion: In our cohort of cluster headache patients, we found no increased prevalence of migraine and epilepsy when compared to figures from the general population. This study does not support a major role of cortical hyperexcitability, as hypothesized in epilepsy and migraine, in cluster headache.

PO132

Cluster headache and other trigeminal autonomic cephalalgias

Effectiveness of sphenopalatine ganglion (SPG) stimulation for cluster headache: 2 year long-term follow-up results from the pathway CH-1 study

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Background: In the randomized, double-blind, multicenter study of an inserted sphenopalatine ganglion (SPG) neurostimulator (Pathway CH-1), 68% of patients experienced clinically significant improvements with SPG stimulation within the 4 month study period.

Aim: To evaluate long-term response to SPG stimulation for chronic cluster headache (CCH).

Method: 43 patients with medically refractory CCH (minimum 4 attacks/week) were enrolled in the Pathway CH-1 study; 33 continued into a long-term follow-up study and completed at least 2 years of follow-up. Each treated attack was evaluated for effective therapy (pain relief from moderate or greater pain, or pain freedom from mild pain). Acute responders achieved effective therapy in $\geq$50% of evaluable treatments. Frequency responders experienced a $\geq$50% reduction in attack frequency compared to baseline.

Results: A total 5956 attacks were treated among all 33 patients (19% mild initial pain, 45% moderate, 23% severe, 13% very severe). 65% (N = 3849/5956) of these attacks achieved effective therapy (64% of mild attacks, 78% of moderate, 62% of severe, 23% of very severe). 61% (20/33) of patients experienced clinically significant improvements, with 5 patients classified as both acute and frequency responders, 10 classified as acute, and 5 classified as frequency responders. Acute responders successfully treated, on average, 75% of their cluster attacks. Frequency responders experienced, on average, an 82% reduction in attack frequency.

Conclusion: SPG stimulation continues to be effective for the treatment of medically refractory CCH in a majority of patients for two years following initial implant.

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Cluster headache and other trigeminal autonomic cephalalgias

Sphenopalatine ganglion (SPG) stimulation in the pathway CH-1 study reduces headache burden in patients before and after sustained periods of cluster attack remission

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Background: The ATI Neurostimulation System applies electrical stimulation to the sphenopalatine ganglion (SPG) to relieve pain associated with cluster headache (CH). Data are presented from Pathway CH-1 study participants who experienced remission from CH attacks.

Aim: To understand acute and/or preventive benefits of SPG stimulation in patients that have experienced remission from CH attacks.

Methods: 33 medically refractory chronic CH-patients participated in the Pathway CH-1 study from pre-implant through 18 months post-implant, with an average CH duration of 10.6 (range 5–17) years. Patients reporting no cluster attacks during the previous 4 weeks were considered to have experienced remission. HIT-6 was used to evaluate headache disability.

Results: 9 patients achieved remission during the study. Pain-free periods lasted an average of 111 days (range

28–268) and began 150 days (range 42–303) into the study. Patients achieved pain relief or freedom in 50.7% (77/152) and 57.3% (110/192) of evaluable attacks before and after remission, respectively. HIT-6 scores improved 16% from baseline and >4X the clinically significant disability improvement. After remission, 5 patients stopped use of acute medications and 4 had clinically significant reductions in their number and/or dose of or remained off preventive medications. All 9 patients indicated they find SPG stimulation useful and would recommend the therapy to other patients.

Conclusion: A subset of CH patients experience long-lasting remission and improved quality of life with SPG stimulation. SPG stimulation may be an effective treatment for medically refractory episodic CH patients.

PO134

Cluster headache and other trigeminal autonomic cephalalgias

Cost-effectiveness analysis of non-invasive vagus nerve stimulation (NVNS) for the treatment of chronic cluster headache in Germany

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Background: Cluster headache is a severe primary headache condition that impacts quality of life and healthcare costs. The Prevention and Acute Treatment of Chronic Cluster Headache (PREVA) study compared adjunctive nVNS (gammaCore®) therapy with the subjects' standard of care (SoC) versus SoC alone. Here we report results from a health economic evaluation of nVNS performed alongside this trial.

Aim: Evaluate the cost-effectiveness of nVNS for the treatment of chronic cluster headache.

Methods: A 1-year model was developed to estimate the cost-effectiveness of nVNS from the German statutory health insurance perspective. Efficacy data and abortive medication use were taken from PREVA, and quality-adjusted life years (QALYs) were estimated using EQ-5D™ utilities. Treatment response beyond 1 month was estimated using survival analyses. Published German costs were used along with the monthly cost of nVNS treatment (€450).

Results: Our model estimated costs of €8,346 and 0.620 QALYs for nVNS+SoC versus €7,930 and 0.532 QALYs for SoC alone. This equates to €4,746 per QALYs gained with nVNS. Results were insensitive to modeling assumptions, including duration of nVNS response.

Conclusions: Healthcare policy makers are typically willing to pay €20,000 per QALY gained for new technologies, indicating that the additional benefits of nVNS (0.09 QALYs over 1 year) would be worth up to €1,800. Because the additional costs in our analysis were estimated at approximately €400, this suggests nVNS is a highly cost-effective treatment. Had we factored in other cost items, eg, decrease in total clinic visits, nVNS therapy would likely have generated further cost savings.

PO135

Cluster headache and other trigeminal autonomic cephalalgias

Regional differences of cluster headache in Brazil

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Background: Regional differences of cluster headache (CH) within an extensive country have not been sufficiently studied.

Aim: To describe differences in the characteristics of CH in all Brazilian regions (North, Northeast, Midwest, Southeast and South).

Method: People from spontaneous demand were included regardless of gender or age, resident in any region of Brazil, fulfilling the diagnostic criteria of CH from the ICHD-II, with informed consent. 998 patients responded to our 40-questions questionnaire throughout 2010–2014, via Internet or written form.

Results: In average, Brazilian Midwest region had the longest diagnostic delay (8,2 years), while Northeast had

the shortest (6,1 years). The Male:Female ratio in once chronic CH was inverted in the Midwest (0,4:1 with p).

Conclusion: Some of the characteristics of CH in Brazil have demonstrated regional differences and the factors associated with them, including medical assistance and those with demographical and geographical origin, should be addressed in further studies.

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Cluster headache and other trigeminal autonomic cephalalgias

Female burden of cluster headache in Brazil

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Background: The decline in male preponderance has brought into light the female burden of cluster headache (CH).

Aim: To describe the characteristics of CH in Brazil influenced by female gender.

Method: People from spontaneous demand were included regardless of gender or age, resident in any region of Brazil, fulfilling the diagnostic criteria of CH from the ICHD-II, with informed consent. 998 patients responded to our 40-questions questionnaire throughout 2010–2014, via Internet or written form.

Results: In average, Brazilian women had earlier onset of CH (24,9 years) than men (26,8 years) with bigger diagnostic delay (8,2 versus 7,4 years). The Male:Female ratio in once chronic CH (1,5:1) was significantly lower than in primary episodic CH (2,8:1 with $p = 0{,}003$). Pain migration to auricular, maxillary, mandibular, occipital and/or cervical areas was significantly more widespread in women ($p < 0{,}001$). All nine migrainous symptoms asked were more prevalent in females; only photophobia and phonophobia were not statistically significant ($p > 0{,}05$). Mean pain duration was longer in women (80,6 minutes) than in men (68,1 minutes), yet 59 (21%) women once had more than eight crises/day, while 73 (10,2%) men once had that ($p < 0{,}001$). Family history of migraine was significantly more frequent in females ($p = 0{,}003$), but excluding these patients did not alter the results to matter. Complaints of depression, anxiety and mood fluctuations were significantly more predominant in women ($p < 0{,}01$).

Conclusion: Most of the characteristics of CH in Brazil were negatively influenced by female gender and further studies are warranted to confirm this, excluding comorbidity with other primary headaches.

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Cluster headache and other trigeminal autonomic cephalalgias

Cluster headache in Brazil: a nationwide survey

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Background: Despite being the most severe pain known to man, our knowledge about cluster headache in Brazil is scarce.

Aim: To describe the characteristics of cluster headache in Brazil.

Method: People from spontaneous demand were included regardless of gender or age, resident in any region of Brazil, fulfilling the diagnostic criteria of cluster headache from the ICHD-II, with informed consent. 998 patients responded to our 40-questions questionnaire throughout 2010–2014, via Internet or written form.

Results: Characteristics of cluster headache in Brazil were similar to those recently found in western populations, like the decline in male preponderance (Male:Female ratio 2,55:1), the prevalence of chronic pattern between 10 and 20% (13,4%), the right side laterality preference (47,6%), predominant orbital pain localization (87,5%), the high prevalence of migrainous symptoms (87,5%) like photophobia, lacrimation as the main autonomic phenomenon (87,8%), the majority of patients with restlessness or inquietude (74,8%), the pain average duration superior to 1 h (71,6 min), nocturnal crisis predominance (00–02 h with 53,6%),the low prevalence of familiar history of cluster headache (8,2%), the smoking (54,6%) and alcoholism (58,5%) prevalence above country's average, the comorbidity with psychiatric symptoms (62,7%) and sleep disturbances (38,4%), and the majority of patients mentioning previous or current treatment (84,8%). The average age of onset was a bit lower (26,3 years), like in the eastern populations, and the seasonality around solstices opposite to the equinoxes of other studies.

Conclusion: Cluster headache in Brazil is similar to what is found in the western literature and the noted differences demand further studies.

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Cluster headache and other trigeminal autonomic cephalalgias

Cognitive dysfunctions are common in cluster headache: a tertiary care headache clinic based study from North India

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Background: Only a few studies of cognitive dysfunctions in cluster headache (CH) have been reported previously. Studying cognitive functions may facilitate better understanding of pathophysiology of CH.

Aim: To assess the occurrence of impairment of attention, vigilance and executive functions in CH.

Methods: CH patients in cluster periods during headache free intervals were prospectively studied after taking written informed consent, by battery of tests including Frontal assessment battery (FAB), Digit span (DS), Stroop colour word interference test, Trail making test (TMT) A and B and P300 event related potentials (ERP).

Results: Twenty nine CH patients (22 ECH and 7 CCH) with mean age 34.5 years and male to female ratio of 1.63 were seen. Average symptom duration was 5.1 years. 25 patients had formal education up to eighth standard or higher, four were illiterates. Therefore, all patients could not perform all the tests. FAB scores were impaired in 75.8% (n = 22/29) patients. All CCH patients had impaired FAB except one. TMT-A was impaired in 29.6% (n = 8/27) and TMT-B in 14.3% (n = 3/21). Forward & backward DS tests were impaired in all patients. In Stroop colour interference test, 17/25 patients (68%) committed errors; their average time was significantly higher (36.2 seconds vs 28.75 seconds) than those who didn't. P300 ERPs done in 12/29 patients showed significant prolonged latencies (mean = 440.95 ms) & lower mean amplitude (mean = 18.17uV) compared to lab normative data.

Conclusion: Cognitive dysfunctions are common in CH patients in cluster period during headache free intervals. Impairment of attention and vigilance is more common than executive dysfunctions.

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Cluster headache and other trigeminal autonomic cephalalgias

Spectrum of psychiatric co-morbidities in cluster headache:experience from a tertiary care headache clinic from north india

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Background: Psychiatric co-morbidities in cluster headache (CH) have received lesser attention. These may have important bearing in their management & quality of life & hence need to be explored.

Aim: To assess the occurrence & spectrum of psychiatric co-morbidities in CH patients.

Methods: CH patients in cluster periods during headache free intervals were prospectively screened for psychiatric co-morbidities by patient health questionnaire followed by detailed instruments for rating specific psychiatric disorders namely Hamilton rating Scale for depression, Generalized anxiety disorder-7 for anxiety, Yale-Brown obsessive compulsive scale for obsessive compulsive disorder, Mood Disorder Questionnaire for bipolar disorder & Anxiety sensitivity index-3 for panic attacks. Written informed consent was taken.

Results: Thirty CH patients (23 episodic CH and 7 chronic CH) with mean age of 37.8 years & male to female ratio of 1.5 were seen. All episodicCH patients were in cluster period. Average symptom duration was 5.7 years. Mean pain intensity was 9.23 on CH rating scale. 16 patients (53.3%) had psychiatric co-morbidity. Specific psychiatric disorders seen were major depression (n = 14; 46.6%), generalized anxiety (n = 11; 36.6%), panic attacks (n = 6; 20%) & somatization disorder (n = 7; 23.3%). 36.6% patients (n = 11) had both depression & anxiety. Suicidal ideation was present in 43.3% patients (n = 13); 3 attempted suicide. 33.3% patients (n = 10) had perception of impending doom during attacks. None had bipolar or obsessive compulsive disorder.

Conclusion: Our study, the first from India on this subject shows that co-morbid psychiatric disorders are common in CH patients during cluster period, depression & anxiety being the commonest. These need identification & treatment for optimum outcome.

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Cluster headache and other trigeminal autonomic cephalalgias

Analysis of a series of 50 adult patients with cluster headache. Demographic, clinical and psychosocial characteristics

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Background: Cluster Headache (CH), the most prevalent trigeminal autonomic cephalalgia (group 3, ICHD-3 beta), is characterized by recurrent attacks of severe pain in periorbital and / or temporal region of 15–180 minutes of duration, with ipsilateral oculo-facial autonomic symptoms and / or restlessness. Although a long known entity, population studies are relatively scarce.

Aim: The aim of this study was to analyze the demographic, clinical and psychosocial characteristics of a series of CH patients.

Method: We present a retrospective study of 50 CH adult patients treated in a Headache Clinic from a University Hospital serving a 350.000 population in Majorca, Spain, between 2004 and 2014. We reviewed their medical records and conducted personal interviews by telephone.

Results: We include 50 patients (43 males) aged between 23 and 82 years (mean 45.2), 30 active smokers, 10 with chronic forms. Some interesting data are: a relatively short time to diagnosis in half of them (<1 year); low degree of suicidal ideation; no dominant laterality; attacks predominantly nocturnal or during naps; low prevalence of vascular disease; and absence of major comorbidity. Alcohol is the most frequent trigger of attacks during symptomatic periods. Six patients with chronic forms and three with episodic ones use oxygen at home.

Conclusion: An important finding is the relatively low number of CH patients treated at this level of medical attention in our area. Some of the data match with those classically described, while others (eg lower diagnostic delay and degree of suicidal ideation) are somehow different.

PO141

Cluster headache and other trigeminal autonomic cephalalgias

Long-term outcome in occipital nerve stimulation in refractory chronic cluster headache

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Background: Cluster headache is considered one of the most painful and disabling primary headaches. About 10–15% of these patients develop the chronic form, of which 10–20% do not respond to any medication. These patients suffering recurrent attacks and result in limitation of lifestyle. Case series suggests that occipital nerve stimulation may be effective in short-term for the treatment of chronic cluster headache.

Aim: To evaluate the long-term efficacy of occipital nerve stimulation in patients with chronic cluster headache unresponsive to pharmacotherapy at our centre.

Method: We present the efficacy, safety and tolerability data of all patients with refractory chronic cluster headache who have been implanted with bilateral occipital nerve stimulator system at our institution from 2006.

Results: Sixteen patients with intractable chronic cluster headache underwent implanted bilateral occipital nerve stimulator. Mean age was 44.75 years (range 25–70 years). Twelve patients were males and four were females. Follow-up range was 1–8 years (mean 4.5). Reduction of disability was: eight patients were pain free, two patients changed to episodic attacks of cluster, four patients had a >50% reduction in number of attacks, one patient persisted in chronic situation and one patient changed to chronic contralateral cluster. Preventive treatment was removed in nine patients. Complications in these patients were: three explants of system, two migrations and three battery replacement.

Conclusion: Occipital nerve stimulation is a useful treatment for refractory chronic cluster headache and maintains its effectiveness for many years. This technique is safe but the rate of complications is high in the long term follow-up.

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Cluster headache and other trigeminal autonomic cephalalgias

Validation of the comprehensive headache-related quality of life questionnaire (CHQQ) in cluster headache: preliminary data

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Background: The Comprehensive Headache-related Quality of life Questionnaire (CHQQ) is a new headache-specific quality of life instrument that had previously been validated in migraine and tension type headache.

Aim: To present the psychometric properties of the CHQQ in cluster headache (CH).

Patients and methods: 60 CH patients (age 39.2 ± 13.3 years; 21 females and 39 males) suffering from episodic CH ($N = 57$) or chronic CH ($N = 3$) completed the CHQQ and the SF-36 generic quality of life questionnaire. The clinical characteristics of the headaches were collected using a structured interview. We assessed the reliability (internal consistency) as well as the criterion, convergent and discriminative validity of the CHQQ. To examine the discriminative validity of the instrument, CH patients' data were compared to those of 177 migraineurs (age: 34.9 ± 11.2 years; 156 females and 21 males).

Results: The CHQQ showed excellent reliability: Cronbach's alpha was 0.922 for the whole instrument, and 0.765–0.843 for its dimensions. CHQQ's dimensions and total score showed significant negative correlations with headache severity and attack frequency (criterion validity), and showed significant positive correlations with most of the the SF-36 domains (convergent validity). The total score and dimensions were significantly ($p < 0.05$) lower in the CH group than in the migraine group (discriminative validity).

Conclusion: The CHQQ showed adequate psychometric properties in this group of cluster headache patients.

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Cluster headache and other trigeminal autonomic cephalalgias

Aggressiveness and impulsiveness in chronic and episodic cluster headache

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Background: Psychological comorbility of cluster headache (CH) has received much less attention than in migraine or tension-type headache. Most of the hypotheses on CH personality characteristics such as those regarding impulsiveness and aggressive behaviour have not been validated by solid observational data.

Aim: The aim of the study was to investigate whether patients with CH have higher levels of aggressiveness and impulsivity compared to healthy volunteers.

Methods: Eighty-one CH patients (72.8 % ECH, 27.2% CCH) attending two headache clinics were asked to fill in the Aggression Questionnaire (AQ, a self-report scale exploring – verbal aggression, physical aggression, anger and hostility) and the Barrett Impulsiveness Scale (BIS, a self-report scale exploring impulsiveness in three different "keys" attentional key, motor and non planning). Data regarding ECH were collected in both the active and remission phase.

Results: Physical aggression scores were significantly higher in CCH than in controls (19 ± 2 vs.14.8 ± 1, $p < 0.05$) whereas anger scores were significantly higher in both active ECH (17 ± 1.2) and CCH (19 ± 2) than in controls (14.8 ± 1, $p = 0.04$). The attentional key scores of BIS were significantly higher in both ECH and CCH patients than in controls (17.8 ± 1, 18 ± 2 and 14.3 ± 1, respectively, $p < 0.0001$). In the 39 ECH patients completing the questionnaire in the active and the remission phase no significant difference was found as regards both AQ and BIS indexes.

Conclusion: Our data suggest the presence of trait-dependent higher levels of aggression and impulsivity in CH patients specifically regarding the physical aggressiveness, anger and the attentional key dimensions.

PO144

Cluster headache and other trigeminal autonomic cephalalgias

Peripheral nerve stimulation (PNS) and periferal nerve field stimulation (PNFS) in the treatment of chronic primary headaches and facial pain syndromes

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Background and objectives: Peripheral nerve stimulation (PNS) and peripheral nerve field stimulation (PNFS) are widely used in the treatment of different pain syndromes. Our study is aimed to demonstrate efficacy of PNS and PNFS in the treatment of chronic facial pain syndromes and chronic primary headaches.

Material and methods: 26 patients (mean age 49 y.o., f/m = 15/11) have bee implanted with test electrodes for stimulation of peripheral nerves and peripheral nerve field. 11 patients suffered from primary headaches: chronic migraine (2 patients), chronic cluster headache (8 patients), and chronic paroxysmal hemicrania (1 patient). 15 patients had neuropathic facial pain. All patients had significant neuropathic pain component, confirmed with DN4, Pain Dtect and, LANSS tests. Pain intensity was assessed with modified Brief Pain Inventory. After test stimulation, 22 patients had been implanted with chronic neurostimulation system.

Results: Mean duration of follow-up was 22 months. In the short-term follow-up (6 months) 7 patients (29%) had more than 90% pain relief, in 17 patients (71%) pain relief varied from 50% to 75% and only one female patient had less than 20% pain relief. In the long-term follow-up 16 patients (67%) reported more than 50% pan relief. All patients with primary headaches had decreased frequency of pain attacks. Analgetic consumption had decreased down to 50% in all the patients.

Conclusion: PNS and PNFS may be concerned as effective technique for the treatment of chronic facial pain syndromes and primary headache. Further investigations are essential to detail predictors of long-term efficiency and mechanisms of clinical effect.

PO145

Cluster headache and other trigeminal autonomic cephalalgias

Indomethacin-induced headache in hemicrania continua: characterization of phenotype and predisposing factors

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Objectives: To characterize the frequency and phenotype of indomethacin-induced headache (IH) in Hemicrania Continua (HC), and identify predisposing factors for the development of IH.

Background: HC is a lateralized headache syndrome marked by a complete therapeutic response to indomethacin. However, headache is a known side effect of indomethacin (e.g., in the treatment of rheumatologic disorders). The nature of IH remains unclear, as is its occurrence in primary headache disorders (including HC).

Methods: This was a retrospective review of all cases of HC seen by the author from September 15, 2012 to December 31, 2014 at the Columbia University Headache Center.

Results: 37 patients were identified meeting ICHD-II criteria for HC. Ten patients (27%) developed a 'new' headache during indomethacin treatment, distinct from their original HC headache. In all cases, the 'new' headache was described as bilateral, throbbing, with bilateral photophobia/phonophobia and nausea. There was a significant association between prior history of episodic migraine and development of IH ($*p = 0.0067$); IH was not seen in any patients without prior history of migraine. A higher maximum indomethacin dose was also associated with IH (203 mg ± 36 *vs.* 156 mg ± 61, $*p = 0.0397$). There was no association between duration of indomethacin use and development of IH ($p > 0.05$).

Conclusion: Indomethacin-induced headache is not uncommon in HC. The phenotype of IH is migrainous, and is associated with a prior history of migraine and higher indomethacin dose (though not duration). The dual effect of indomethacin may be a function of its nitrergic properties, and affirms the nosologic distinction between these headache syndromes.

PO146

Cluster headache and other trigeminal autonomic cephalalgias

Onabotulotoxin a for the treatment of chronic paroxysmal hemicrania: a case report

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Introduction: Chronic paroxysmal hemicrania (CPH) is characterized by attacks of very severe, unilateral pain, fulfilling the criteria of The International Classification of Headache Disorders, 3rdedition, beta version (ICHD-3 beta) for paroxysmal hemicrania andoccurring without a remission period, or with remissions lasting < 1 month,for at least 1 year.

Aims: OnabotulinumtoxinA isnow used for the treatment of chronic migraine. We wanted to try the treatmentof CPH with OnabotulinumtoxinA,because other treatments have not been effective.

Patient and Method: Wepresent the case of a patient diagnosed with CPH that lasts for 32 years. Attacks of headache lasted about 15 years without remission. The patient described her headaches asattacks of hemicrania-lasting from 15 to 25 minutes with a frequency of usually 8times per day. OnabotulinumtoxinA wasadministered at nineipsilateral points. The total dose was 45 units (each intramuscular injectionsite was 0.1 mL = 5 U onabotulinumtoxinA). Eight points were identical as in the treatment of chronic migraine in thefrontal and temporal areas and one point was in infraorbitalarea. Method was application of onabotulinumtoxinA based on the methodology of application of onabotulinumtoxinA inpatients with chronic migraine.

Results: TheCPH showed a dramatic response to onabotulinumtoxinAinfiltration. The effect of the treatment was evident as early as three weeksafter the first injection, gradually improved, it takes eleven months fromstart of treatment with 3-monthly infiltrations.

Conclusions: Thetreatment of CPH with Onabotulinumtoxin Asignificantly improved the quality of life of the patient.

PO147

Cluster headache and other trigeminal autonomic cephalalgias

Cluster headache in Greece: a case series of 81 consecutive patients

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Background: Characterized by a lengthy episodic or even chronic history of disabling episodes of significant pain, cluster headache (CH), affecting an estimated 0.1% of the general population in western countries, is an important neurologic problem. Up to date, no data on cluster headache in Greece have been published.

Aim: To present data on clinical characteristics of a case series of CH patients from Greece.

Method: Consecutive CH patients (n = 290) were recruited from our specialist clinic between 2007 and 2014. All patients had a detailed history taken and were assigned diagnoses according to the International Headache Society (IHS) diagnostic criteria. During the analysis phase, the III beta version of the criteria was used. Data from 81 consecutive patients have been fully analysed and are presented here.

Results: Most patients were male (80.25%) and suffered from episodic CH (70.4% vs % 25.9 chronic and 3.7% probable CH). Mean age of CH onset was 32.8 years (minimum 13 and maximum 67 years). Pain was strictly unilateral but side shift between and within bouts was reported by 6.2% and 2.5%, respectively. Typically pain was most commonly present in the retro-orbital (93.8%), temporal (72.9%) and forehead (48.1%) region, but interestingly location of maximum pain was in neither of these regions in 19.7% of cases. Lacrimation (87,7%) was the most common autonomic symptom. Photophobia (65%), phonophobia (41%) and nausea (27%) were often noted.

Conclusion: Patients with CH in Greece follow the internationally described stereotyped clinical presentation of the disease.

PO148

Cluster headache and other trigeminal autonomic cephalalgias

Diagnostic delays and mismanagement in cluster headache in Greece

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Background: Despite its stereotyped clinical presentation, cluster headache (CH) is often misdiagnosed or its diagnosis is delayed. Up to date, no relevant data from Greece have been published.

Aim: To present data on diagnostic delays and mismanagement in a large case series of CH patients from Greece.

Method: Consecutive CH patients (n = 290) were recruited from our specialist clinic between 2007 and 2014. All patients had a detailed history taken and were assigned diagnoses according to the International Headache Society (IHS) diagnostic criteria. During the analysis phase, the III beta version of the criteria was used. Data from 81 consecutive patients have been fully analysed and are presented here.

Results: Among 81 patients, 30 had already been diagnosed in the past, while 51 were previously undiagnosed or misdiagnosed. Mean age of CH onset was 32.8 years, while mean age of diagnosis was 40.3 years. Forty-nine percent of total patients were diagnosed with migraine at some time in the past. Mean time from onset to CH diagnosis was 8.1 years (minimum 0, maximum 41). The vast majority of undiagnosed patients had consulted a physician in the past (86%, mean number of physicians consulted: 3.4). The majority consulted a primary care physician (80%), but 33% a neurologist. Among undiagnosed patients 12% underwent dental and ENT surgical procedures in the past. Correct self-diagnosis, primarily through the internet, was done by 16% of patients.

Conclusion: Our data indicate a significant issue in prompt diagnosis and management of CH in Greece.

PO149

Cluster headache and other trigeminal autonomic cephalalgias

Hemicrania continua in association with other pathologies: a critical review of published cases

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Background: Hemicrania continua is a rare primary headache disorder. According to the ICHD-3 beta criteria, it is characterised by constant side-locked headache for >3 months, accompanied by ipsilateral autonomic symptoms and responding absolutely to indomethacin. A number of patients presenting with a hemicrania continua-like syndrome co-existing with or attributed to other pathologies have been presented. Consequently, for the evaluation of the possible causal relationship between unilateral headaches and coexisting conditions, sets of criteria have been proposed.

Aim: We aimed to critically review all published cases of secondary hemicrania continua according to the degree of fulfilment of the ICHD-3 beta criteria and in addition to evaluate the possible causal relationship between the headache and the co-existing pathology.

Method: A PubMed search identified 23 published cases. Only cases with detailed data available were included in our review. All cases were independently reviewed by the two authors.

Results: Nine out of 23 cases fulfil the diagnostic criteria for hemicrania continua completely and 5 more to a great extent. In 14 cases a causal relationship between the coexisting pathology and the headache symptoms seems plausible, out of which 6 cases are bona fide "secondary hemicrania continua".

Conclusion: Absolute concordance with the diagnostic criteria for hemicrania continua does not necessarily infer a primary aetiology; when prompted so by the remaining clinical presentation, further diagnostic work-up is advised.

PO151

Cluster headache and other trigeminal autonomic cephalalgias

Comparative evaluation of the treatments of the 2nd-division of primary trigeminal neuralgia by percutaneous radiofrequency thermocoagulation through the pterygopalatine fossa or the foramen ovale

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Background: The percutaneous radiofrequency thermocoagulation (PRT) of the Gasserian ganglion through the foramen ovale (FO) approach for the 2nd-division of primary trigeminal neuralgia (TN) could be at risk of the destruction of the 1st-division TN. In order to avoid the risk, the PRT through the pterygopalatine fossa (PF) approach could be performed.

Aim: To compare with using PRT through PF or FO in patients with the 2nd- division of TN in terms of the efficacy duration of pain relief, side effects and complications.

Methods: 96 patients from two different pain management centers were enrolled into this study and randomly divided into two groups. Patients in group A underwent PRT with the PF approach, and in group B with the FO approach. Baseline characteristics of the patients, immediate outcome, duration pain-free, side effects and complications were obtained from their medical records and questionnaires. Duration pain-free was assessed by Kaplan–Meier analysis.

Results: The average follow-up time was 47.1 ± 34.2 months. Immediate success rates of PRT in groups A was 88.0% (44/50), and group B was 91.3% (42/46). Patients in both groups experienced excellent pain relief after the procedures. The mean duration of excellent pain relief in group A and group B was comparable, whereas the rate of complication in group A was 6% and that in group B was 26.1% ($P < 0.05$).

Conclusion: Performing both approaches can achieve pain relief for the 2nd division of TN, whereas the approach of PF can be safer than that of FO.

PO152

Cluster headache and other trigeminal autonomic cephalalgias

Lamotrigine as first line treatment in sunct headache

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Introduction: SUNCT (Short-lasting Unilateral Neuralgiform headache with Conjunctival injection and Tearing) is considered worldwide refractory to treatment useful in other TAC (Trigeminal-Autonomic Cephalalgias) or neuralgias. Most cases or series are described as difficult-to-treat and with poor outcome. Our aim is to describe a series of patients and their long-term outcome after treatment with lamotrigine.

Methods: Series of 8 patients: 5 males, 3 females. Age between 17–67 years. A secondary SUNCT in a patient after pituitary surgery, the rest are primary. All patients received 100–400 mg lamotrigine as preventive treatment. We describe the response to lamotrigine and long-term outcome (mean follow-up 5 years).

Results: Excellent response to lamotrigine in 5 patients; 2 acceptable partial response; one little response. Symptomatic periods are shorter than those described in the literature, the majority of patients without recurrence (single period). We found no chronic / untreatable cases. A case with seizures triggered by the SUNCT attack in an epileptic patient with cannabis consumption (SUNCTalepsia?). Not all patients had attakc triggers.

Conclusions: SUNCT headache may be underdiagnosed, especially benign cases.

The natural history of the disease does not seem so bad if all cases are considered and not just rebels or refractory ones.

The response to lamotrigine has been very good in our experience, we propose it as a first line treatment in SUNCT patients.

PO153

Cluster headache and other trigeminal autonomic cephalalgias

Therapeutic effectiveness of sphenopalatine ganglion (SPG) stimulation for cluster headache – pathway registry study interim results at 6 months

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Background: The Pathway Registry is an open label registry of sphenopalatine ganglion (SPG) stimulation for cluster headache (CH). In a randomized, double-blind, multicenter study (Pathway CH-1), 68% of medically refractory patients experienced clinically significant improvements.

Aim: The aim of this interim analysis is to evaluate acute and/or preventive therapeutic effectiveness at 6 months following insertion of an SPG neurostimulator.

Method: Therapeutic effectiveness (acute pain response following SPG stimulation and/or attack frequency reduction) was analyzed during the first six months following SPG neurostimulator insertion. Acute pain responders achieved pain relief from moderate or greater pain, or pain freedom from mild pain in $\geq$50% of analyzable attacks (with completed diary questions). Frequency responders achieved $\geq$50% attack frequency reduction at the six month study visit (evaluated over previous four weeks), versus the 4 week baseline.

Results: 83 patients were enrolled and underwent implantation; as of December 2014, complete data through six months follow-up (191 days post-insertion, range 153–238) had been received for 39 patients. Average baseline attack frequency was 23.0 attacks/week (range 0–70); average attack frequency at 6 months was 17.8 attacks/week (range 0–70). One patient was attack free at baseline, remained attack free at 6 months, and was not analyzed. 61% (23/38) were responders. Of responders, 52% (N = 12) were acute responders, treating 88% of 1545 attacks effectively. 70% (N = 16) were frequency responders; frequency reduced by 86% on average. 5 patients were both acute and frequency responders.

Conclusion: Interim data from a cluster headache patient registry continues to demonstrate effectiveness of SPG stimulation.

PO154

Cluster headache and other trigeminal autonomic cephalalgias

Cluster headache and pituitary adenylate cyclase-activating polypeptide-38 – preliminary results

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Background: Cluster type headache (CH) is a primary, trigeminal autonomic headache disorder. The periodically occurring unilateral, severe attacks are accompanied by intense vegetative symptoms due to the overactivity of cranial parasympathetic system. Its exact pathomechanism is still unknown, but the role of trigeminovascular and hypothalamic systems are proved. In our previous work we have demonstrated the involvement of pituitary adenylate cyclase-activating polypeptide-38 (PACAP-38) in the mechanisms of migraine.

Aims: Our goal is to determine the PACAP-38 plasma levels in the interictal and ictal periods of patients suffering from CH.

Methods: We have enrolled 9 male CH patients according to the international guidelines of headache diseases. Age and sex matched healthy subjects were also recruited. Blood samples were taken from the cubital veins from the control volunteers and in the interictal and ictal periods of patients. Concentrations of plasma PACAP-38 were measured with radioimmunoassay.

Results: Significantly lower plasma PACAP-38 level was detected in the attack-free period of patients (25.10 ± 4.51) as compared with the healthy control subjects (28.98 ± 4.30) ($p < 0.04$). However, significantly higher plasma PACAP-38 concentration was detected in the ictal period (27.80 ± 1.44) as compared with the interictal phase (24.37 ± 3.30) ($p < 0.03$).

Conclusion: These preliminary results suggest that during the attacks the PACAP-38-containing trigeminal and parasympathetic fibers can release the amount of peptide, which can contribute to the development of CH due to its direct/indirect sensitizing effects. Further patients and long-term follow-up are needed to reveal the function of PACAP-38 in the mechanism of CH.

TAMOP-4.2.2.A-11/1/KONV-2012-0052, NAP-KTIA-13-NAP-A-III/9, NAP-B-KTIA-NAP-13-2014-0022-888819, EUROHEADPAIN-FP7-Health 2013-Innovation-602633, MTA-SZTE Neuroscience Research Group.

PO155

Cluster headache and other trigeminal autonomic cephalalgias

Anodal transcranial direct stimulation (tDCS) targeting the anterior cingulate gyrus for the preventive treatment of chronic cluster headache: a proof-of-concept trial

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Background: There is a need for better treatments in chronic cluster headache (CCH). In responders to percutaneous occipital nerve stimulation the subgenual anterior cingulate gyrus was found hypermetabolic (Magis et al. 2011). We reasoned that activation of this area by transcranial neurostimulation could be effective in CCH.

Aim: To explore the preventive effect of anodal (i.e. activating) transcranial direct current stimulation (tDCS) targeting the anterior cingulate gyrus in CCH patients.

Method & subjects: CCH patients applied tDCS (2mA) daily for 20 minutes during 4 weeks with anode positioned over the forehead (FpZ), and cathode over C7. Therapeutic effects were monitored with paper diaries.

Results: Nine CCH patients were enrolled up to now: 7 completed the trial, 2 were not satisfied and dropped out. In evaluable patients mean weekly attack frequency decreased by 44% after 3 weeks (W-test: $p = 0.03$) and by 34% after 4 weeks ($n = 6$; W-test: $p = 0.04$). Four weeks after the last stimulation, attacks had decreased by 73% ($n = 5$).

The first 3 enrolled patients had superficial skin burns under the adhesive cathode electrode. Sponge electrodes were used for all subsequent patients without any adverse effect.

This study is ongoing and will include 20 patients.

Conclusion: Anodal tDCS targeting the anterior cingulate gyrus may be promising for the preventive treatment of chronic cluster headache according to the interim results of this ongoing proof-of-concept study. The use of adhesive electrodes is not recommended.

Acknowledgements: this trial was funded by the Fondation Roi Baudouin, devices provided by Cefaly Technology®.

PO156

Cluster headache and other trigeminal autonomic cephalalgias

Cluster headache secondary to gamma knife radiosurgery

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Background: Cluster Headache is the most frequent type of trigeminal autonomic cephalalgias with a prevalence of 0.1%. Most cases are primary cluster headache although symptomatic cluster headache due to intracranial pituitary masses, meningiomas and aneurysms have been reported.

Aim: We report a case of new onset cluster headache following gamma knife radiosurgery for medically refractory trigeminal neuralgia.

Method: A 73 year old woman with multiple sclerosis and a twelve year history of left maxillary and mandibular

distribution trigeminal neuralgia underwent gamma knife radiosurgery. Her typical trigeminal neuralgia related pain resolved post procedure. Nightly since the gamma knife radiosurgery she experienced a sharp stabbing pain to the left temporal region with ipsilateral lacrimation and rhinorrhea occurring between 2 and 4 am each morning typically lasting 3 hours. Prednisone at 50 mg daily was effective to prevent the headache, at lower doses symptoms returned. The frequency of acute episodes decreased with Verapamil at 80 mg 3 times daily to 2 episodes per week. Sumatriptan Nasal Spray 5 mg/ACT used at the onset of pain produced pain freedom within 30 minutes.

Conclusion: Trigeminal neuralgia is a well known complication of multiple sclerosis secondary to a demyelinating lesion of the trigeminal sensitive fibers located in the nerve root or the brainstem. In our patient's case the gamma knife radiosurgery may have triggered cluster headaches secondary to activation of the trigeminovascular system and the presence of autonomic signs may be related to activation of the central autonomic reflexes suggested to be involved in CH pathogenesis.

PO157

Cluster headache and other trigeminal autonomic cephalalgias

The use of botulinum toxin type a in the treatment of trigeminal cephalgia

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Introduction: The purpose of the report demonstrate the effectiveness botulinoterapii in patients with trigeminal cephalgia against the backdrop of compression vessels.

In the pilot group studied 4 patients with trigeminal cephalgia. All patients had defeated two pairs of the trigeminal nerve. Pain syndrome on VAS scale was 4 points. During the attack of pain 9 points. All patients had sleep disturbance, anxiety, asthenia. The average duration of the trigeminal cephalgia patients group was 5 years old. As treatment, patients received a dose of pregabalin 400–600 mg per day.

All patients were administered botulinum toxin type A 30 units subcutaneously in the trigger zone and the area of irradiation of pain on his face. Efficacy of the treatment was assessed after 7 and 21 days. After 7 days the pain VAS decreased in the period from 9 to attack balls 7. After 21 days in three patients the pain syndrome regressed completely. One patient remained pain VAS 2 points.

Conclusions: Thus, botulinum toxin type A was effective in the treatment of trigeminal cephalgia and can be considered as a promising method of treatment of this pathology.

PO158

Other primary headache disorders

Primary headache associated with sexual activity. A case report

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Headaches provoked by triggering factors have been recognized for many decades. In many cases, the development of such headaches is secondary to an underlying pathology. However, in some cases, no abnormality can be identified. Primary headache associated with sexual activity (PHASA) is one of the subgroup of primary headaches. PHASA is a benign form of headache and lifetime prevalence estimated to be 1–1.6 % in the general population. A 38-year-old man was admitted to our outpatient clinic reporting a history of severe headache during sexual intercourse for the last 2 months. He was experiencing headache bilaterally in occipital area just after orgasm and then it lasted about in 2 hours. He was started on propranolol 40 mg/ day, on follow up which he noted a dramatic improvement in two weeks, and treatment was maintained for six months. He has been on regular follow-up for a year, and his headache did not repeat. This is a rare case PHASA. In this patient, prophylactic treatment with low dosage of propranolol was successful.

PO159

Other primary headache disorders

Transient paroxysmal stabbing headache

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The diagnostic criteria of primary stabbing headache (PSH) has refined recently in ICHD-3. As the spectrum of PSH is enlarged, we investigated clinical outcome of transient paroxysmal stabbing headache (PaSH). Among the subjects referred to Kangdong Sacred Heart Hospital presenting with PaSH of acute-onset during the last 5 years, two hundred and thirty patients in which their headache has spontaneously resolved within 2 weeks were retrospectively included. We analyzed clinical characteristics such as dermatome distribution, VAS score, seasonal effects and etc. At the initial presentation, all patients were neurologically and physically normal. The most prevalent location was lesser occipital nerve dermatome (46%), followed by greater occipital (28.5%), V1 (11.4%), V2(8.7%), and V3(1.3%) dermatomes. 40 patients(17.5%) involved multiple dermatomes during the course. Out of 228 patients, 45 patients suffered from allodynia and 15 patients complained of tenderness at the point. During the course, Bell's palsy developed in 2 patients and cephalic or cervical zoster lesions developed in 7 patients. Those with unknown etiology, 45 patients reported stressful events and 23 patients had upper respiratory tract infection. 69 patients had past history of similar headache. Conclusions : Most patients with transient PaSH of acute-onset meet criteria of the ICHD-3 diagnostic criteria of PSH. The most prevalent location of PSH was lesser occipital nerve dermatome. However, the possibility of impending Bell's palsy or Herpes zoster infections should be considered in the diagnosis.

PO161

Other primary headache disorders

Trochlear headache. First three mexican cases

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Objective: To report the first Mexican series of this condition.

Case 1: 69 y/o female, SAH, DM and dyslipidemia. Three months with unilateral retroocular pain with no visual complains; daily, 7/10 VAS, worst in the morning. Pain elicited on pressure of the internal- superior orbital wall that worsened on infra-endoversion. MRI of brain and orbits reported normal. Response of 100% to indomethacin.

Case 2: 54 y/o female evaluated because of a 10 years history of generalized pain, headache and continuous ocular pain. Multiple unsuccessful treatments. Diagnosed with severe fibromyalgia, occipital neuralgias. The ocular pain worsened on pressure to the internal-upper orbital wall with the eye on infra-endoversion. Trochlear infiltration with lidocaine-betametasone abolished the pain. Three years later a Crohn's disease was detected. Occipital neuralgias were cured with infiltration. Currently on chronic treatment with tapentadol.

Case 3: 30 y/o male previously healthy evaluated because of frontal headache. One year with continuous pain with up and downs, periocular, unilateral, penetrating type, with no response to common analgesics. Clinical exam showed pain on pressure to the internal-upper orbital wall with worsening on infra-endoversion. Indomethacin induced remission with recurrence 10 months later. Trochlear Infiltration with lidocaine – betamethasone disappeared the pain.

Discussion: Trochlear headache is attributed to inflammation of trochlear-peritrochlear tissues. Now it is known there are primary and secondary forms. Response to indomethacin in two cases is worth to mention. As far as we know, this is the first Latin American series.

PO162

Other primary headache disorders

Seasonal variation, cranial autonomic symptoms, and functional disability in migraine

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Background: Cranial autonomic symptoms (CAS) seen in trigeminal autonomic cephalalgia are also present in a subset of patients with migraine. Seasonal variation of headache attack, a characteristic of cluster headache, is reported in migraine as well. We hypothesized that CAS is more prominent in migraineurs with seasonal variation than those without.

Aim: This study aimed to identify distinct clinical features including CAS and evaluate functional disability in this subset of migraineurs.

Methods: We conducted a questionnaire-based study on patients with migraine without aura who visited our institution from January 2005 to December 2013. Patient demographics, headache characteristics, and accompanying symptoms were recorded, and functional disability was evaluated by Migraine Disability Assessment (MIDAS) Questionnaire.

Results: A total of 769 patients were included in the analysis, and 104 (13.5%) of them reported seasonal variation of headache. CAS and several other migraine-associated symptoms were more prominent in this subset of patients. They showed higher MIDAS scores than the other migraineurs, with 1.77-fold increased risk (95% confidence interval 1.06–2.96) of severe functional disability (MIDAS score >21) after adjustment for age group, sex, headache frequency, intensity, and duration. Intriguingly, the proportion of patients with severe functional disability also increased with the number of CAS.

Conclusions: The association of CAS with seasonal variation in migraine suggests a pathogenic overlap in migraine and cluster headache. The profound functional disability in the migraineurs with CAS or seasonal variation also provides direction for proactive clinical management in these patients.

PO163

Other primary headache disorders

Association between neurovascular contact and clinical characteristics in classical trigeminal neuralgia: a prospective clinical study using 3.0 tesla MRI

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Background: Previous studies demonstrated that a severe neurovascular contact (NVC) causing displacement or atrophy of the trigeminal nerve is highly associated with classical trigeminal neuralgia (TN).

Aim: We aimed to describe the association between the clinical characteristics of TN and severe NVC. We hypothesized that the neuroanatomical abnormalities would be different in men and women and that severe NVC on the symptomatic side was associated to age and duration of disease.

Methods: Clinical characteristics were prospectively collected from consecutive TN patients with unilateral pain using standardized semi-structured questionnaires in a cross-sectional study design. 3.0 Tesla MRI imaging was conducted according to a special protocol and evaluated by a blinded neuroradiologist.

Results: We included 135 TN patients. Severe NVC was more prevalent in men (75%) compared to women (38%) ($p < 0.001$) and the odds in favor of severe NVC on the symptomatic side were 5.1 times higher in men compared to women (95%CI 2.3–10.9, $p < 0.001$). There was no difference between patients with and without severe NVC in current age (≥60 years vs. <60) (OR 1.6 95%CI (0.8–3.4), $p = 0.199$), duration of disease ($p = 0.101$) or in the prevalence of concomitant persistent pain ($p = 0.201$) or sensory abnormalities at bedside examination ($p = 0.408$).

Conclusions: Severe NVC was much more prevalent in men than in women who may more often have other disease etiologies causing or contributing to TN. Severe NVC was not associated to age or to duration of disease.

PO164

Other primary headache disorders

Headache and cervical related disabilities are associated in migraine patients

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Background: Migraine causes substantial disability for patients and their families. The presence of cervical pain is highly frequent in migraine patients. However, the contribution of neck pain to the overall disability experienced by migraine sufferers has received little attention.

Aim: To investigate the association between disability due to cervical pain and to headache in patients with migraine.

Methods: Patients with migraine who also suffered from cervical pain for at least 3 months were recruited from a university-based center. Migraine was diagnosed by experienced neurologists according to Second Edition of the International Classification of Headache Disorders

(ICHD-II). Exclusion criteria included history of trauma at the cranio-cervical region, cervical radiculopathies and/or spine degenerative disease. Migraine disability was assessed with the Migraine Disability Assessment (MIDAS), whereas cervical pain-associated disability was assessed with Neck Disability Index (NDI). Pearson's correlation coefficients were used to determine correlations between the NDI and MIDAS scores in univariate analysis. Correlation was classified as weak (<0.30), moderate (between 0.30 and 0.70), or strong (>0.70).

Results: Forty-three women (mean age: 34, SD: 10) with a mean headache frequency of 12 days per month (SD: 9.2) were included. A positive and moderate correlation between cervical-pain and headache related disability was observed (r: 0.63; 95%CI 0.41– 0.78; $P < 0.05$). Individuals with high MIDAS scores were also likely to score high in the NDI.

Conclusion: We observed that headache and neck pain disability were associated in migraine.

PO165

Other primary headache disorders

Relationship between head and cervical posture and neck disability in patients with migraine

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Background: The prevalence of neck pain in patients with migraine is high and sometimes associated with dysfunction in the neuromuscular function. One of the cervical spine impairments most commonly seen is head postural changes.

Aim: To examine the relationship between head and cervical posture and the neck pain-related disability in individuals with migraine.

Methods: The sample consisted of 50 subjects (45 women), age 34 (95%CI 31–37) years, with migraine diagnosed by a neurologist according to the ICHDIII[1]. These subjects had no history of cervical injury, disc herniation or physiotherapy treatment in the last year. A radiograph of the sagittal cranio-cervical region was taken in all subjects to examine head/neck posture. By using K-Pacs® software, four specific angles[2–4] (°) and four specific distances[3–5] (mm) were measured in each radiograph. Neck pain-related disability was assessed with the Neck Disability Index[6] (NDI – 0: no disability; 50: high disability). Pearson's correlation coefficient between the angles, distances and the NDI were calculated.

Results: Seventy-eight percent of the migraine patients exhibited neck pain. Our sample of patients showed mild disability: mean NDI score 11.9 (95%IC 9.9–13.8). One angle (C2-C7PT: $R = -0.13$, $P = 0.03$) and 2 distances (C0-C1D: $R = -0.15$, $P = 0.02$; HT: $R = -0.20$, $P = 0.01$) were negatively correlated with the NDI: the higher the neck pain-related disability, the smaller the C2-C7PT angle and the smaller the C0-C1D and HT distances.

Conclusion: Some weak negative correlations between cervical posture and neck pain-related disability were found. Clinical significance of the relationships needs to be elucidated.

PO166

Other primary headache disorders

The study of validity of duloxetine/mirtazapine to chronic primary headache with depressive state

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Introduction: We medicated chronic primary headache with depressive state with duloxetine or mirtazapine and examined the validity to improve of headache, depressive state, apathy and anxiety.

Object: We examined 8 chronic headache patients(5 chronic migraine: ICHD-3β1.3 and 3 chronic tension-type headache: ICHD-3β2.3). We medicated six patients with duloxetine 20 mg/day and medicated two patients with mirtazapine 40 mg/day for eight weeks. Before and after medication, we examined MINI(DSM-IV), Hamilton Depression Scale(HAM-D) for evaluation of depressive state, apathy and anxiety and Visual Analog Scale for evaluation of pain (VAS).

Result: In all cases, headache has improved, and MINI, HAM-D and VAS became significant improvement with that. In addition, we analyzed to sub items of HAM-D. As the results, depressive state, apathy and anxiety has

improved with improvement of a headache. Furthermore in all cases, there were not side effects including dysuria.

Discussion: As for amitriptyline which is one of the Tricyclic Antidepressants (TCA) is established the evidence as a prophylactic of Chronic headache.

Both duloxetine and mirtazapine accelerate promptly increases of secretion in both serotonin and noradrenaline. Thereby, improvement of serotonin and noradrenaline depletion and activating descending pain inhibitory system may cause improvement of chronic headaches. These results suggests that duloxetine and mirtazapine may also be one of the useful option in the treatment of Chronic primary headache with depressive state.

PO167

Other primary headache disorders

Botulinum toxin type a in trigeminal neuralgia

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Trigeminal neuralgia is an unilateral pain with a electric dicharge, short, that appears and disappears briefly, limited to one or more division from trigeminal nerve, and burst by innocuos stimuli. The treatment of choice is with antiepileptic drugs, and no smaller group of patients are intolerant or decreased therapeutic effect to them after a while.

Surgical treatment, may be an alternative for patients who do not respond to medications o if finds neurovascular conflict. There are contraindicated patients having surgery or have recurrent pain after the same.

Botulinum Toxin type A has been shown in migraine and others neuralgias beneficial resuls.

Aim: To evaluate the benefit and safety on botulinum toxim type A in patient whit classical and secondary trigeminal neuralgia refractory to treatment.

Methods: Observational work in 25 patients with refractory neuralgia to conventional therapy of betwen 20 and 85 years.

Onabotulinum toxin was injected betwen 40 and 70 subunits skin, following the pain.

They were assessed with VAS, frecuency and patient global impression of change scale, to 1st and 2nd month.

Result: Of 25 patients, 13 are classic, 12 secondary. The 2nd month 17 VAS improved in 7–8 points 68%, frecuency and global impression improve 15,60%, 18 were able to reduce medication 72%. No improvement 8 32%. 15 were are reinfltrated.

Conclusion: TBA could be a benefical option and safe as minimamly invasive treatment for trigeminal neuralgia and other facial-skull pains refractory to conventional treatments.

PO168

Other primary headache disorders

The effective use of gliacin for the treatment of primary cough headache

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Background: Indomethacin is generally considered to be the drug of choice for primary cough headache (PCH). Although indomethacin can be extremely effective, it's often associated with serious side effects like gastrointestinal bleeding. Gliacin™ is a novel, patent-pending, derivative of *Boswellia serrata* that has been previously proposed to be a safer, better-tolerated substitute for indomethacin.

Aim: Review the cases of nine patients who responded to Gliacin™ for the treatment of primary cough headache (PCH)

Methods: A case series of nine patients with PCH (based on the ICHD-3 [beta] criteria) who have been successfully treated with Gliacin™ is reported.

Results: All nine patients (eight men and one woman; 39 to 60 years of age) with PCH experienced dramatic initial improvement with indomethacin. Because of serious side effects, all patients willingly converted to Gliacin™ and took doses ranging from 1,125 mg to 3,375 mg per day. All nine patients quickly became Gliacin™ responders as well. Only one of the patients experienced side effects ("mild indigestion") with Gliacin™. All patients preferred Gliacin™ over indomethacin and all but one (who combines both therapies) were able to entirely discontinue indomethacin. No adverse reactions have been associated thus far with long term (120 total patient months) Gliacin™ use.

Conclusions: In this case series, Gliacin™ has been used to successfully treat nine patients suffering from PCH. Gliacin™ was well tolerated, preferred over indomethacin and cost effective. Gliacin™ represents the first herbal

preparation used to successfully treat PCH and its use warrants further investigation.

PO169

Other primary headache disorders

Upper cervical spine mobility in migraine patients

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Migraine is a severe primary headache triggered by the trigeminovascular system activation and is often accompanied by neck pain that may affect the cervical range of motion, especially in the upper cervical spine. The aim of this study was to investigate the mobility of C1/C2 vertebral segments using the Flexion Rotation Test (FRT) in chronic and episodic migraine patients. 45 women were recruited and divided into three groups: chronic migraine (CM), episodic migraine (EM) and without headache (WH) with mean age of 36.40 ± 9.52, 33.53 ± 10.54, 25 ± 6.41 years old respectively. The volunteers were diagnosed by neurologists according to the ICHD-III (3ed.) and a blind evaluator assessed the upper cervical mobility with the FRT. The average range of motion for the CM, EM and WH groups for the rotation to the right was respectively 27.38°, 34.36° and 46.76°, to the left rotation was 27.47°, 34.18°and 44°. Range of rotation was significantly reduced in the CM group when compared to groups EM and WH groups ($P < 0.05$). The EM group had a smaller amplitude compared to the WH group ($P < 0.005$). These findings support the idea that migraine patients presents dysfunction in the upper cervical spine with a decreased mobility of the vertebral segment C1 / C2 similar to found in patients with cervicogenic headache.

PO170

Other primary headache disorders

The physiotherapy participation in a multidisciplinary team on the headache outpatient clinic: experience report

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Headaches cause severe dysfunctions and a multidisciplinary treatment has been appointed as the best approach for these patients. In a headache outpatient clinic, neurologists are responsible for establish the diagnosis of headache according to the ICHD-III (3ed.) and develop pharmacological treatment plans, while physiotherapists are trained to recognize which disorders of musculoskeletal system are contributing to the patient's symptoms. The aim of this study is report the experience of physiotherapy inclusion in a multidisciplinary team. The team consists of three neurologists, eight residents in neurology, a psychologist, a dentist, five physiotherapists and eight undergraduate physiotherapy. Physiotherapists accompany consultations and when requested they participate in assessment and orientation of patients to self-care in pain management, postural adjustments and performing relaxation. When necessary some patients are referred to be followed in the Headache and Temporomandibular Disorders Physiotherapy Service, particularly those with myofascial impairment, migraine or other headaches with neck pain, cervicogenic headache or restriction on use of medication. Since February 2009, the physiotherapy evaluation was requested for 303 patients and until August 2014, 2262 were assisted. In addition, the patients were recruited for clinical research that resulted in 12 full papers in scientific journals, 52 abstracts published at national and international conferences, 9 works of scientific initiation, three masters, one doctorate and post-doctorate thesis. A multidisciplinary approach is often recommended and considered highly relevant in the care of patients with headache, and the presence of physiotherapist is beneficial to improve the clinical management and production of knowledge in the field.

PO171

Other primary headache disorders

Features of cerebrospinal fluid dynamic disorders in patients with initially chronic viral encephalitis

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Methods: MRI head, spinal cord, research of cerebrospinal fluid and its dynamic, immunological researches.

Results: At an estimation of the received data of general content of IgE in blood serum the following parameters of the food allergy were considered: 0 – absence or below a threshold [0,00–0,34 IU/ml], 1 – threshold level [0,35–0,69 IU/ml], 2 – moderately increased [0,70–3,49 IU/ml], 3 – considerably increased [3,50–17,49 IU/ml], 4 – high [17,5–49,9 IU/ml], 5 – very high [50,0–100 IU/ml], 6 – exclusively high level [>100,0 IU/ml]. Thus it is necessary to underline, that threshold level was regarded by us as a fact of presence of a food allergy at patients MS, which indicators (the general IgE) could accrue, especially at increase of available clinical symptoms MS or occurrence of the new symptoms. Thus changes of immunogram indicators simultaneously took place. Among 23 patients with MS surveyed by us, the food allergy is revealed in 4 people (17,4 %). It has allowed to exclude the application of glucosteroid therapy, which is counter-indicative and not safe for patients and to appoint the effective pathogenetic treatment including antiallergic, antihistamine preparations in a combination with probiotics (linex, etc.).

Conclusion: At formation of the program of medical rehabilitation of patients with MS it is necessary to consider not only activity of demyelination process, but also to exclude food allergy presence. It is necessary to exclude also the use of multicomponent dishes by patients with MS with a food allergy.

Keywords: multiple sclerosis, rehabilitation, food allergy

PO172

Other primary headache disorders

Indomethacin test usage at united kingdom tertiary centres over 20 years- an audit

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Background: Indomethacin-responsive trigeminal autonomic cephalalagias (TACS), paroxysmal hemicrania (PH) and hemicrania continua (HC), are unique, important syndromes to understand.

Aim: Evaluation of the role of the placebo-controlled indomethacin test (P-Indotest) in the diagnosis of primary headache disorders.

Method: Patients notes, clinic letters and headache diaries of patients under our care (PJG) over a 20 year period across various UK Neurology tertiary care centres were examined to obtain data against an audit collection tool. A pre-determined set of data were extracted, and the test procedure reviewed for compliance against a standard with minimum data set requirement by an unblinded observer. The original test score was noted, and prospectively re-scored by a blinded observer.

Results: Patients (n = 7; 4 female) were aged from 24 to 51 years. The majority (85%) had side locked headache. P-Indotest was positive in 78% of the cases with patients having either HC or PH. Of all patients tested, 42% had unilateral photophobia and phonophobia and all these cases had a positive response. No serious adverse events were noted. Sleepiness was often reported on the active treatment as was transient worsening of headache in unilateral chronic migraine. Further data is being compiled.

Conclusion: The P-IndoTest is a reliable and safe test and should in the diagnosis of patients with possible indomethacin sensitive TACs. While far from ideal, a positive indomethacin test does identify a particular biology and should be retained as a diagnostic marker of PH and HC until its basis is understood.

PO173

Other primary headache disorders

Trigeminal neuralgia – introduction and implementation of a new coherent work-up and treatment regime

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Background: Diagnosis and treatment of patients with classical trigeminal neuralgia (TN) lies in the hands of both medical and surgical specialties. Lack of knowledge regarding treatment strategies and the severe pain intensity render clinical management of TN challenging.

Aims: To describe the implementation of a seamless and accelerated treatment regime for TN patients at the Danish Headache Center (DHC) and to report the flow of patients during the first year after implementation of the regime.

Methods: The first out-patient visit was booked 4–6 weeks after referral. Patients initially referred to the department of neurosurgery were re-directed to DHC for pre-surgical evaluation of diagnosis and optimization of medical treatment. A 3.0 Tesla MRI scan was performed within 6 weeks. Patients were followed for at least two years with four fixed out-patient visits where medical treatment was adjusted and the need for referral to neurosurgery was evaluated (Figure 1).

Results: From May 2012 to April 2013, 72 patients entered the accelerated regime. Of these 64% continued medical treatment during the following year, while 36% where referred to neurosurgery (Figure 2). Initial feedback from patients and clinicians about the program was very positive.

Conclusion: The newly implemented accelerated regime outlined here represents, according to initial feedback from patients and clinicians, a marked improvement of our TN treatment.

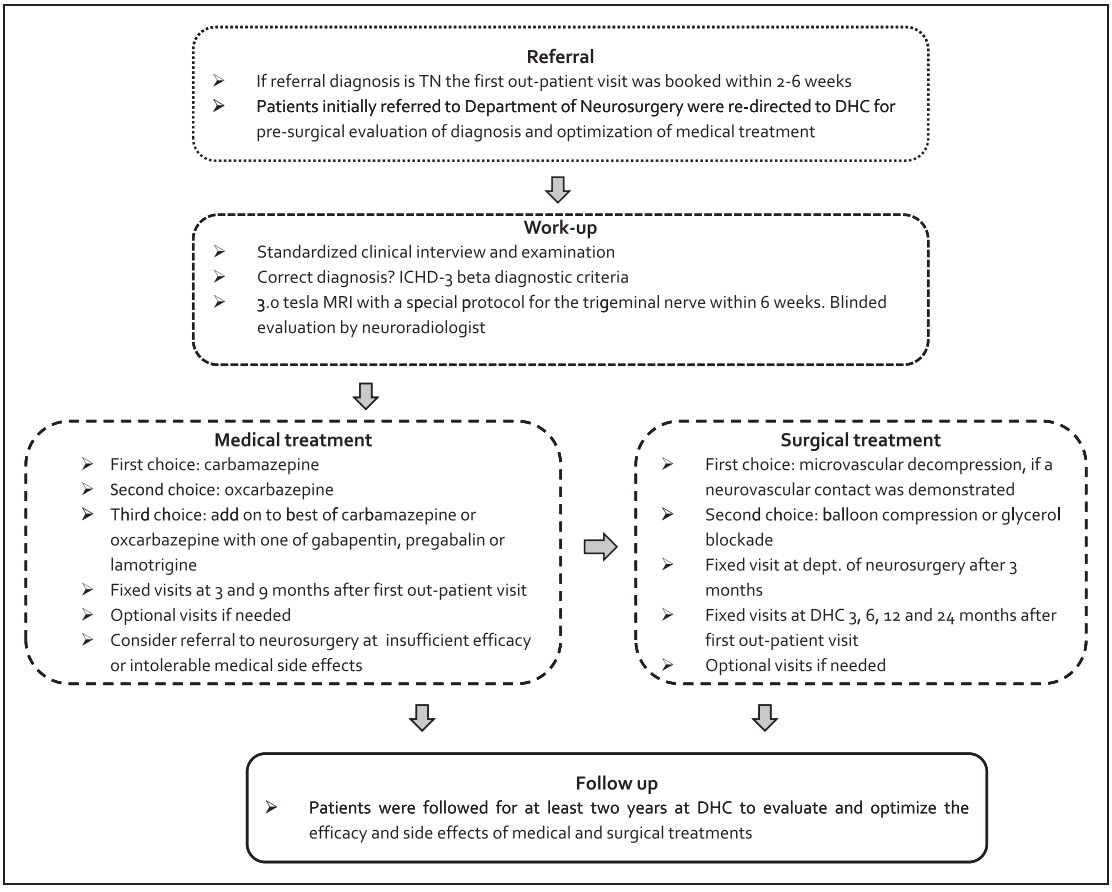

Figure 1. Algorithm of work-up and treatment of patients with Trigeminal neuralgia at the Danish Headache Center (DHC).

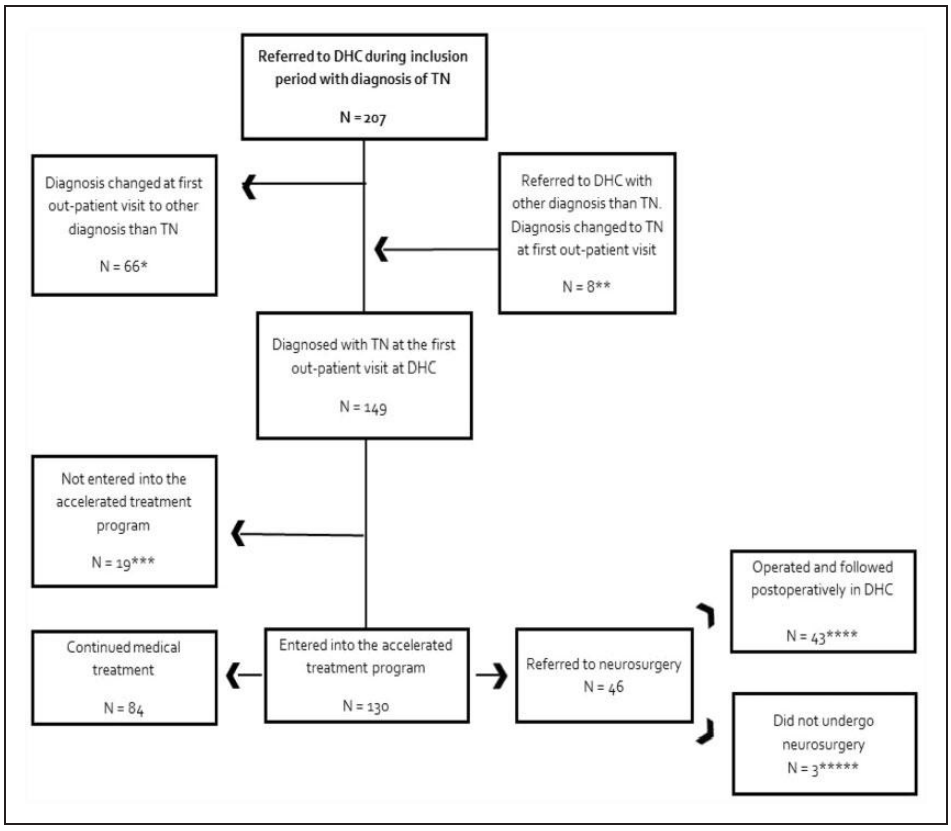

Figure 2. Flowchart of patients and diagnoses at the Danish Headache Center (DHC) in the inclusion period.

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Other primary headache disorders

Headaches associated with physical exertion – headache center belgrade

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Headaches provoked by physical effort (HAPE) are rare primary headache disorders with unresolved pathogenesis and without treatment recommendations. Careful examination with appropriate tests are necessary because of high number of secondary cases. During thirteen years, 72 patients with HAPE (1.5% of all patients) were examined in our Headache Center. Headache provoked by coughing, sneezing, straining or laughing was present in 19 patients. The majority of these patients (70%) were older than 40 years, and secondary headaches were diagnosed in 38.6% of the patients: Arnold-Chiari malformation type I, primary intracranial hypertension, ethmoidal or sphenoidal sinusitis, and intracranial aneurysm. Headache provoked by exercises were diagnosed in 29 patients, but in 6 of them migraine with or without aura or tension-type headache were provoked by this type of physical exertion. Secondary headache were diagnosed in 3 patients from this group, most often Arnold-Chiari malformation type I. More than 70% of patients were males, and in half of them the onset was during adolescence. Typical headache provoked by exercises was severe and pulsating, lasting from few seconds do 72 hours, and associated in the third of patients with photophobia, phonophobia, nausea and vomiting. Headache provoked by sexual activity was diagnosed in 29 patients, secondary in 17.2% of patients. The majority of the patients were males, aged between 17 and 58 years. Abrupt explosive intensity with pulsating quality localized in occipital region and lasting 1–30 minutes were typical features for the headache. Thunderclap headache was the most often presentation in this group of patients.

PO175

Other primary headache disorders

Long term outcomes in hypnic headache syndrome: 32 patient series from a tertiary referral center

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Objective: We retrospectively identified 32 hypnic headache cases at a tertiary headache referral center over the course of 6 years and assessed response to conventional treatments.

Methods: Patients were identified using ICD-9 diagnostic codes of hypnic headaches (339.81) from October 2008 until September 2014 using the ICHD II and III-beta criteria for diagnosis. Primary outcome was response to medications divided into 4 categories: complete response (headaches completely gone), moderate response ($\geq$50% decrease in frequency), partial response ($<$50% decrease in frequency), no response.

Results: Thirty-two (32) patients (86% females) were identified with hypnic headaches. Average age of headache onset was 62 years (range 44–83). Nineteen patient had previous history of migraine (59%), 31% vitamin D deficiency, and 50% underlying sleep abnormalities. Ninety percent (90%) of patients were awakened between 1:00 and 5:00 AM with headache. The average duration per day and frequency per month of headaches was 193 minutes (range 45–720 minutes) and 21 days (range 5–30) respectively. Mean follow-up was 3.1 years (range 1.5–85 months). Among 13 different medications tried, the best response was seen with lithium [7/10 (70%) complete response and 2/10 (20%) moderate response]. With caffeine, there was a complete response in 5/17 (29%) and moderate response in 6/18 (33%) subjects. Patients in the bedtime caffeine group also benefited from taking a caffeinated drink at the time of awakening.

Conclusions: Lithium is the most effective treatment option in patients with hypnic headaches. Caffeine at the time of awakening may also be a beneficial option for headache relief.

PO176

Other primary headache disorders

Migrainous retinopathy: reduced RNFL thickness in patients with migraine

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Background: In patients with migraine, vasospasm has been shown to occur in the tissues outside the brain, especially in the retina layer, concurrent with a reduction in brain blood flow. Since migraine attacks are recurrent and associated vasospasm is transient, It could lead to alteration in the perfusion of retinal head microcirculation and even retina proper causing ganglion cell death and reduction in RNFL thickness.

Aim: To assess Retinal Nerve Fibre Layer Thickness (RNFL) by Optical Coherence Tomography in patients with migraine.

Methods: 24 patients of migraine were recruited according to IHS classification and were subjected to measurement of retinal nerve fiber layer thickness by OCT. RNFL thickness were considered abnormal if Average RNFL thickness was $<$100 micrometers, Superior quadrant thickness $<$120, Temporal $<$ 80, Nasal $<$ 80, Inferior $<$ 120.

Results: Among 24 patients [3 male (12.5%), 21 female (87.5%)], 3 patients (12.5%) had aura and 21 patients (87.5%) had no aura. Among 24 patients, 5 patients (20.8%) had duration of headache for 2–4 years, 17 patients (70.8%) had $>$4 years. Among 24 Patients, 10 patients (54.2%) had 5–10 episodes/month and 2(8.3%) had $>$10 episodes/month. Among 24 patients, 8 patients (33.3%) had 2–24 hours/episode and 11(45.8%) had $>$24 hours/episode. RNFL thickness was reduced in 18 patients (75%) in right eye in right temporal quadrant and it was reduced in 20 patients (83.3%) in left eye in left temporal quadrant.

Conclusion: Migraine produces changes in RNFL, predominantly in the temporal quadrant of both eyes.

Keywords: Migraine, Retinal nerve fibre layer thickness, Optical coherence tomography

PO177

Other primary headache disorders

ECG changes in patients with migraine

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Background: Autonomic system involvement responsible for many clinical features of migraine leads to derangement of circulatory system and autonomic balance. This imbalance causes atrial and ventricular repolarisation abnormalities and arrhythmias. These marked autonomic derangements during ictal period produces changes within heart and coronary vessels which may cause ECG abnormalities in the form of cQT interval and P-wave changes which may be predictors of atrial and ventricular arrhythmias.

Aim: To assess of ECG changes in migraine both during attack and pain free periods.

Method: Patients with migraine were recruited according to International Headache Society classification from Madras institute of neurology, India. ECG variables of heart rate, Abnormalities of rhythm, P wave duration, PR interval, QRS duration, QT interval, corrected QT interval (cQT), ST changes and T wave inversion were analysed in migraine patients both during ictal and nonictal periods.

Results: Out of 50 patients with migraine [males(12%), females (88%), 34 ictal(68%), 16 nonictal(32%)], 4 had arrhythmias in the form of ventricular premature complexes (8%), 26 had T wave Inversion(52%),19 had ST changes (38%), 21 had abnormal P wave duration $>$.10 sec(42%), 4had abnormal cQT interval(8%) and 1 had abnormal PR interval of $>$.20 sec(2%). In ictal group, 17 patients(50%) had abnormal ST changes, 23(67.6%) had abnormal T inversion and 13(38.2%) had abnormal P wave duration. Only values in the ictal group for ST changes and T wave inversion were statistically significant(P value .011, .001).

Conclusion: We conclude that ECG abnormalities are often noted in migraine patients. Further studies are needed to correlate ECG manifestations and occurrence of arrhythmias.

Keywords: ECG, Migraine

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Other primary headache disorders

Visual evoked potentials in patients with migraine

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Background: In patients with migraine vasospasm is known to occur. Since migraine attacks are recurrent and transient, it can cause structural alteration in the visual pathway which could lead to changes in visual evoked potentials.

Aim: To assess pattern reversal visual evoked potentials (PR-VEP) in patients with migraine both during ictal and nonictal period.

Method: 39 Patients [6 male (15.4%), 33 female (84.6%), 28 ictal (71.8%), 11 nonictal (28.2%)] were recruited from Madras institute of neurology, India and were subjected to Pattern Reversal Visual Evoked potentials PR-VEP). P100 amplitude is considered to be abnormal if $>$110 milliseconds and abnormal P100-N75 amplitude if $<$10 microvolts.

Results: Among 39 patients, 16(41%) had abnormal P100 latency and 38(97.4%) had abnormal P100-N75 amplitude on right side.11(28.2%) had abnormal P100 latency and 37(97.9%) had abnormal P100-N75 amplitude on left side. Among ictal group (71.8%), 15(53.6%) had abnormal P100 latency and 27(96.4%) had abnormal P100-N75 amplitude on right side and 10(35%) had abnormal P100 latency and 27(96.4%) had abnormal P100-N75 amplitude on left side. Changes in P100 latency are statistically significant(P value.011).

Conclusion: Among migraine patients, Ictal group may have more P100 latency prolongation and amplitude reduction than in nonictal group and abnormal P100 latency is statistically significant.

Keywords: Migraine, Visual Evoked Potentials

PO179

Other primary headache disorders

EEG changes in patients with migraine

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Background: Migraine is associated with a variety of electroencephalographic changes. The purpose of this study is to evaluate EEG manifestations in migraineurs.

Aim: To assess EEG findings in patients with migraine both during ictal and nonictal period.

Method: 25 Patients (3 males and 23 females) with migraine both during ictal and non ictal periods were recruited according to International Headache Society classification from Madras institute of neurology, India and were subjected to standard scalp electroencephalography. The EEG was studied in the awake state at rest, during photic stimulation and during hyperventilation.

Results: 18 patients were recorded during ictal period and 7 patients during nonictal period.19 patients had Focal theta waves and 16 patients had theta waves during HV. 17 patients had focal delta waves. 5 patients had FIRDA (focal intermittent rhythmic delta activity) and 4 patients had FIRDA during HV.3 patients had AIHA (alpha interhemispheric asymmetry). 12 patients had depressed background activity (DBA). Focal theta waves, delta waves, theta waves during HV and Depressed background activity were more in ictal than nonictal patients(88.9% vs 42.9%,77.8% vs 42.9%,72.2% vs 42.9%,55.6% vs 28.6%). These changes were statistically not significant.

Conclusion: Migraine patients may have more EEG abnormality during ictal period than nonictal period.

Keywords: Electroencephalography, Focal intermittent rhythmic delta activity, Alpha interhemispheric asymmetry.

PO181

Other primary headache disorders

Long latency potential in patients with migraine

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Background: P300 is a time-locked measure of electrical activity of the cerebral surface representing a distinct phase of cortical processing and bear special importance to stimulus evaluation, selective attention, and conscious discrimination in humans. In this study we evaluate these three components with P300 in migraineurs to assess differences both during ictal and nonictal period.

Aim: To assess P300 long latency potentials in patients with migraine both during ictal and nonictal period.

Method: 37 Patients [6 male (16.2%), 31 female (83.8%), 3 with aura(8.1%),34 without aura(91.9%), 27 ictal (78%), 10 nonictal (27%)] were recruited according to International Headache Society classification from Madras Institute of neurology, India and were subjected to long latency potential P300.

Results: Among 37 patients [27 ictal(73%), 10 nonictal(27%)] 8 patients(21.6%) had migraine for 2–4 years,15 (40.5%) for 4–10 years,11(29.7%) >10 years duration. And among 37 patients, 11(29.7%) had <5 migraine episodes/month, 24(64.9%) had 5–10 episodes/month and 2(5.4%) had >10 episodes/month. In patients with migraine, 18(48.6%) had 4–24 hours of headache/episode, 14(37.8%) had >24 hours/episode. P300 latency was prolonged >300 ms in 22(59.5%) out of 37 patients. In ictal group P300 latency was prolonged in 17 patients (63%) and 5 patients (50%) in nonictal group.

Conclusion: P300 latency may be prolonged in patients with migraine and mostly during ictal period.

Keywords: P300, Migraine

PO182

Other primary headache disorders

Occipital nerve stimulation in highly refractory chronic headaches: identification of possible predictors of success

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Introduction: Occipital nerve stimulation (ONS) has emerged as a promising treatment for refractory chronic headaches. The procedure is invasive and expensive while response rates vary between studies. Identification of clinical predictors of outcome is therefore of great clinical relevance.

Aim: To prospectively assess the efficacy of ONS in a cohort of intractable chronic headache patients and to identify clinical predictors of response.

Methods: 165 patients undergoing ONS at a single centre between 2007–2013 were studied. Headache load (2 week $\sum$(attack duration [hours] x attack severity [verbal rating score]) was calculated at baseline and final follow-up. A positive response was defined as a 30% reduction in headache load. A multivariate logistic regression analysis was carried out to identify possible predictors of outcome.

Results: Patient group was highly refractory at baseline and 22% suffered from multiple headache types. At a mean follow up of 40 months ($\pm$28 months) the response rate of the group was 50%. Clinical factors identified with an increased likelihood of response were co-existent chronic migraine and chronic cluster (OR 4.44, $p = 0.04$) and the presence of non-headache related pain disorders (OR 2.08; $p = 0.05$). Occipital pain was associated with a reduced likelihood of response (OR 0.44, $p = 0.04$). Adverse event rates were favourable compared to previous reports.

Conclusion: ONS appears to be a potentially useful and safe treatment in highly refractory chronic headache disorders. The presence of multiple pain syndromes appears associated with increased likelihood of response and presence of occipital pain with a reduced likelihood.

PO184

Other primary headache disorders

Efficacy of multiple cranial nerve blocks in primary headache syndromes: a prospective open label analysis

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Introduction: Greater occipital nerve block (GONB) is an establishedtreatment in headache management. Multiple cranial nerve blocks (MCNB) of the supra-orbital,supra-trochlear, auriculo-temporal and greater/lesser occipital nerves are anoption for those patients failing to respond to GONB.

Aim: To prospectively assess the efficacy and side effect profileof MCNB in a cohort of primary headache patients.

Methods: Patients in our unit failing to respond to GONB who werethen treated with MCNB were prospectively studied. Data on headache characteristics werecollected using headache diaries recorded before and after the MCNB. Adverse event data was also collected. A positive response to treatment was taken asa 50% or more reduction of headache load for at least ten days post-procedure. Headache load was calculated using the formula $\sum$ (attack duration [hours] xattack severity [verbal rating score]).

Results: 102 MCNB procedures were analysed. A response was observed in 54% ($n = 55$) of MCNBwith 30% ($n = 31$) resulting in pain freedom at ten days. Response rates by phenotype are shown in Table 1. The mean duration of response was 44 days (range 10–261 days). 45% ($n = 26$) of those who had no response to anyGONB showed a positive response to MCNB. There was a transient worsening of headache in 6% and immediate buttransient dizziness reported after 17% of procedures.

Conclusion: MCNB appears to be an efficacious and well-toleratedtransitional treatment in headache patients and is a treatment option in patients failing to respond to GONB.

PO185

Other primary headache disorders

The prevalence and the clinical profile of primary exercise headache on japanese physical check-up

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Purpose: We aimed to examine the prevalence and the clinical profile of primary exercise headache (PEH) on physical check-up.

Methods: Middle-aged subjects offered health check-up between 2005 and 2007 in PL Tokyo Health Care Center, Japan. A headache specialist (K.I.) interviewed, and the primary headaches were diagnosed according to

the criteria of ICHD-II. Overall prevalence and the clinical features of PEH were assessed.

Results: A total of 2,546 subjects (1,588 men and 958 women) were participated. Twenty-nine subjects (12 men and 17 women) were diagnosed as PEH. The prevalence of PEH was 1.14%, 0.76 in men and 1.77 in women. The mean duration (SD) of PEH was 4.4 (6.9) months. The persistent time of an attack was 5 minutes to12 hours. Headache occurred bilaterally (22 patients) or unilaterally (7), and the occipital region (15), the frontal portion (10) or diffuse region (4). The severity of headache revealed mild degree (12 patients), moderate degree (5) and severe degree (12). PEH-triggered exercises were gym training (12 patients), swimming (6), running (6) and ski (2). All patients were exercise beginners or played a sport occasionally. Twenty patients had migraine without aura (MO). Seven patients had headache associated with sexual activity (HASA). Five patients had cough headache (CH).

Conclusion: The present study indicated the prevalence of 1.14% and the female/male ratio of 2.3 in middle-aged Japanese. The comorbidity rate of MO, HASA and CH was 69%, 24 and 17, respectively. PEH might not be an uncommon headache in middle-aged migraineurs or sport beginners.

PO186

Other primary headache disorders

Chronic migraine and depression are main predictors of cutanoeus allodynia in migraine patients: a hospital-based study

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Introduction: Cutanoeus allodynia (CA) may be involved in associations between depression, headache chronification and treatment failure in migraine patients. We assessed the frequency of and risk factors for CA among migraine patients visiting a tertiary care hospital in Korea.

Methods: Subjects were recruited from a headache clinic and competed self-report questionnaires including a migraine related symptoms, an allodynia symptom checklist (ASC) and headache disability. A physician assessed psychiatric interview was performed with each patients with migraine to assess depressive and anxiety disorders based on the Mini-International Neuropsychiatric Interview (M.I.N.I).

Results: Among 271 migraine patients that completed a study, 38 (17%) had a symptom of CA. The risk of CA in migraine patients was associated with concurrent medical diseases, chronic migraine (CM), medication-overuse headache, longer headache attack duration, higher VAS_{max}, phonophobia, photophobia, higher MIDAS score, depression and anxiety.

Predictors of allodynia in migraine patients were identified using multiple logistic regression analyses. The strongest predictor was depression (OR = 4.055, 95% CI 1.839–8.938, p = 0.001), followed chronic migraine (OR = 3.312, 95% CI 1.403–7.818, p = 0.006), photophobia (OR = 3.191, 95% CI 1.384–7.358, p = 0.006), and headache attack duration (OR = 1.016, 95% CI 1.003–1.028, p = 0.014). Patients with CM and depression concurrently showed a trend of higher grade of allodynia than those with CM or depression alone. (p = 0.003)

Conclusions: In migraine patients in Korea, CM and depression may provoke CA and also associated with the severity of allodynia.

PO187

Other primary headache disorders

Clinical picture of vestibular migraine: characteristics in a series of 26 cases

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Background: Vestibular Migraine (VM) has been included in the appendix of the International Classification of Headache Disorders (ICHD-III). Diagnostic criteria proposed include vestibular symptoms of moderate to severe intensity, associating headache with migrainous features, visual aura or photo-phonophobia.

Aim: To analyze a prospective series of 26 cases.

Methods: Consecutive patients attended from January 2014 to February 2015 in an outpatient headache office were included. We assessed age at inclusion, age at onset of migraine and VM, and intensity, duration and characteristics of vestibular symptoms. Patients with other vestibular disorders were excluded.

Results:26 patients (17 females, 9 males). Age at inclusion was 28.1 ± 12.2 years (14–52), at migraine onset 18.9 ± 9.3 (7–46) and at VM onset 23.7 ± 10.9 (7–46). Seven patients (26.9%) fulfilled diagnosed of chronic migraine and one (3.8%) presented visual aura. Vestibular symptoms were rated as severe by only 2 patients (7.7%) and occurred in 85 ± 21.4% (40–100) of migraine attacks. Duration of episodes was quite variable; in 6 cases (23.1%) lasted 1–5 minutes, in 9 (34.6%) 5–60 minutes and in 8 (30.8%) 1–24 hours. Vertigo was described as internal in 8 patients (30.8%), external in 17 (65.4%) and both internal an external in one (3.8%). In 9 cases (34.6%) vertigo was spontaneous, in 21 (80.8%) positional and in 12 (46.2%) motion-induced. Aural fullness (19.2%) and tinnitus (34.6%) were common accompanying symptoms.

Conclusion: VM is not uncommon in a headache office. In our series vestibular symptoms do not prevent daily activities and are mainly positional and motion-induced.

PO188

Other primary headache disorders

Drug overuse and chronic headaches in Brazzaville: patients profile and therapeutic itinerary

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Medication overuse headache (MOH), is the least studied type of headaches in Africa. In order to report Brazzaville experience, we conducted a longitudinal study for 4 years, from September 2010 to August 2014, in neurology consultation in Brazzaville. Inclusion criteria were patients with chronic primary headache classified according to ICHD 2. Patients were divided into two groups: those who have progressed to MOH, and those who do not have drug abuse criteria. The variables were demographic, the characteristics of the original primary headache and management of MOH. On 212 patients enrolled, 193 constituted our study population. The mean age 42 ± 14 years, of which 66.32% were women. The frequency of MOH was 35.75%. The identified factors associated were: younger age ($p = 0.003$), use of NSAIDand paracetamol ($p = 0.0001$), and self-medication ($p < 0.0001$). Contrariwise, the higher educational level ($p < 0.0001$) and the use of the NSAID alone (0.002) were protective against MOH.

MOHs are common in Africa neurology consultation, and should be identified for better management.

Table 1. Multivariate analysis

Variables	Patients with MOH (n = 69)	Patients Without MOH (n = 124)	OR [IC 95%]	p
Mean age	37 ± 12	44 ± 11	1.68 [1.21–3.12]	0.003
Femal	51(73.9%)	77(62.1%)	1.26 [0.82–2.33]	0.09
Level of education				
Primary	13(18.8%)	15(12.1%)	1.32 [0.46–2.58]	0.36
Secondary	34(49.3%)	47(37.9%)	1.53 [0.65–3.43]	0.42
Higher	18(26.1%)	62(50%)	0.31 [0.12–0.73]	<0.0001
Medicines used				
Paracetamol	11(15.9%)	21(16.9%)	1.04 [0.49–2.11]	0.48
NSAID	13(18.8%)	38(30.6%)	0.69 [0.57–0.94]	0.002
Ergot*	13(18.8%)	15(12.1%)	1.81 [0.69–2.84]	0.67
Paracetamol + Tramadol	6(8.7%)	8(6.5%)	1.54 [0.65–3.45]	0.52
Paracetamol + Codeine	8(11.6%)	21(16.9%)	0.87 [0.52–2.33]	0.12
NSAID + Paracetamol	26(37.7%)	26(20.2%)	2.11 [1.24–3.16]	0.0001

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Other primary headache disorders

Clinical features of self-reported hypnic headache – an internet based survey

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Background: Hypnic Headache (HH) literature contains 70 publications with original data, yet this condition is present in 1% of our Headache Clinic attenders.

Aim: To expand the worldwide dataset on clinical features of HH using an internet survey of Self-Reported Hypnic Headache (SRHH).

Methods: Form posted on www.severe-headache-expert.com for 16 months. Descriptive statistics to compare findings with published literature (147 cases).

Results: 80 surveys completed from 9780 website visitors over 16 months. 30/80 SRHH reported confirmation of diagnosis by Health Professionals. Compared to published cases, SRHH were more likely to be female (10 F:1 M), younger (57 v 64 years), have fewer attacks (17 v 25 nights/month), longer attacks (105 v 61 mins), and took longer to get to a diagnosis from symptom onset (3 v 2.2 years). 12% SRHH had previous migraine, and mean HIT6 score was 59. 6 SRHH cases reported HH in a first degree relative. 21/80 reported an antecedent infection, vaccination or injury to SRHH. 197 different behaviours were reported by 60 people including rubbing head or neck, getting up from lying, agitation, wanting to eat or drink. 20/60 reported staying in bed during an attack instead of being compelled to get up.

Conclusions: Notwithstanding limitations of a self administered survey, there is potential for internet-based headache epidemiological research of rare headaches. A significant number of people with unreported HH self manage as they may have a less severe manifestation than cases seeking medical advice. Prospective population-based studies of HH would clarify clinical features and outcomes.

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Other primary headache disorders

Medication overuse headache (MOH) in clinical sample of primary headaches

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Background: Medication Overuse Headache (MOH), a well-known condition, is a relevant medical and socio-economic problem everywhere. Whether headache type, frequency, co-morbidity or else is crucial in MOH, it is not truly clear.

Aims: We wanted to outline the frequency and some clinical characteristics of patients with MOH, compared with others in the group of primary headaches.

Methods: In a clinical sample of 130 adult out-patients, diagnosed according to ICHD-III Classification, we emphasized a group of patients with MOH and compare them with those without MOH, according to: type of primary headache (migraine an tension type headache), duration of illness, frequency of attacks (headache days per month) and co-morbid depression (HAMD-scale).

Results: In a sample of 130 out-patients, 18–65 years of age, females 101, males 29, 20 patients (15.38%) suffered of MOH. Migraine was diagnosed in 15 (75%) in MOH-group and in 80 subjects (72.73%) in the others, tension type headache: in 5 (25%) in MOH-group and 30 (27.27%) in the others. Average duration of the illness among MOH-patients was 24.65 years and 16.45 years in those without MOH. Headache frequency was 20.50/30 in MOH- and 11.87/30 in non-MOH-group. We found depression in 10 subjects (50%) in MOH- and 54 (49.09%) in non-MOH-group.

Conclusions: MOH headache was presented in 15.38% among all primary headaches. Migraine and tension type headache ratio, as well as depression-rate, were similar in MOH- and non-MOH-group. But, patients with MOH had longer headache life-period and more frequent attacks than those with only primary headache.

PO191

Other primary headache disorders

A chronic form of primary headache with increased tension features and cerebrospinal fluid (CSF) unexplained high protein: case series

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Background: Late onset primary headache disorders are uncommon presentation. High CSF protein usually denotes an inflammatory pathology, either infective or non-infective. Syndrome of transient headache with neurological deficits and CSF Lymphocytosis (HaNDL) has been recognised, with mean duration of 5–19 hours and consistent Lymphocytosis in CSF.

Aim: Presenting three challenging cases of persistent headache (2–6 weeks), with high intracranial features, and high CSF protein, thorough investigations have excluded a secondary cause.

Case Description: Two females (age 49, 67, both diabetic and hypercholestraemic) and one male (46, only on statin) presented all with their first acute headache. MRI Brain/MRA were normal in all along with other systemic blood inflammatory markers. Headache was occipital, worse with leaning forward, sneezing or coughing, and associated nausea in all, with papilloedema in the 2 ladies, and induced by physical exercise and sexual orgasm in the man. All had full orientation, no motor weakness, two had diffuse abnormal sensation, but none showed meningeal signs or restriction of neck movement. CSF showed lymphocytosis (inflammatory) only in one patient but high opening pressure (26–37.5 cm CSF) and high protein (0.86–1.4 g/L) documented in all, each having CSF repeated twice, headaches improved after LP. CSF infective markers including viral, bacterial, and atypical infections were negative in all. No treatment was given and symptoms resolved within 2–6 weeks with brief infrequent recurrence.

Conclusion: In contrary to HaNDL, these patients' headache showed increased intracranial tension not migrainous features, lasted longer, weeks not hours, with consistent high CSF protein and pressure.

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Other primary headache disorders

Onabotulinumtoxin a for the treatment of nummular headache: results in a series of 17 cases

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Background: Nummular headache (NH) is a pain felt in a small, sharply contoured area of the scalp. Preventive therapy may be needed in some patients. Gabapentin, lamotrigine, tricyclic antidepressants, topiramate or carbamazepine have been used with no consistent results. OnabotulinumtoxinA (OnabotA) has been suggested as an alternative in patients with inadequate response to other therapies.

Aim: To assess effectiveness and safety of OnabotA injections in a series of 17 patients with NH.

Methods: Consecutive patients with NH (ICHD-III criteria) in two headache units during a two-year period (January 2013 – January 2015). We recorded age at inclusion and onset of NH and previous preventatives used in each patient. Patients were injected with 10 to 50 units of OnabotA distributed in several points over the symptomatic area. We analyzed changes in baseline pain and exacerbations.

Results: Seventeen patients (15 females, 2 males) were included. Mean age at the first procedure was 54.8 ± 18.6 years (32–85), and latency from onset of symptoms was 3.2 ± 3.6 years (1–15). Four patients (23.5%) had trophic changes inside the painful area. All patients had been unresponsive to 1 to 3 preventatives, mainly gabapentin and lamotrigine. After the first procedure a reduction of at least 50% in basal pain and/or exacerbations was achieved in 15 patients (88.2%). Pain relief lasted at least 12 weeks and was consistent after repeated procedures. No treatment-related adverse effects were reported.

Conclusion: OnabotA, even used in low doses, might be a secure and effective therapy in NH patients.

PO193

Other primary headache disorders

Assessment of effectiveness of clonazepam in patients with burning mouth syndrome

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Background: Different drugs have been studied to treat BurningMouth Syndrome (BMS), Clonazepam, is the only drug thathas been proved to be effective in controlled trials. However, there is controversywithin the authors of its effectiveness and the use of systemic or suckedadministration.

Aim: To assess the effectiveness ofClonazepam in BMS patients followed up for 2 and 6 months.

Method: Retrospective study abouteffectiveness of Clonazepam tablets (1 mg) in 72 SBA patients, according to IHScriteria (los de 2004). Tablets were sucked after each meal for three minutes. Weassessed pain by using the Brief Pain Inventory before the beginning and 2 and6 months after the treatment.

Results: 30.6%of the patients referred reduction of the 50% of the pain 2 months after thebeginning of the treatment and the 38.9% showed the same reduction 6 monthsafter treatment. The 16.7% of the patients were asymptomatic 6 months aftertreatment and 4.2% showed no pain but referred other symptoms as xerostomia.

16.67%of patients experienced decreased xerostomia sensation (58.33% of themhad xerostomia at the beginning of the burning pain) and 33.33% reduced tastealterations 2 months after the beginning of the treatment (58.33% of themhad taste alterations at the beginning).

Conclusion: We conclude that Clonazepam (sucked) is effective in BMS patientsreducing the pain, and other symptoms such as xerostomia and tastedisturbances.

PO194

Other primary headache disorders

Headache, amnesia and sexual activity

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A 54-year-old man, with PMH of episodic migraine without aura, presented with a severe explosive headache at the moment of orgasm, lasting for 3 minutes. Thereafter, the patient experienced a moderate anterograde amnesia that resolved after 3 hours spontaneusly, documented in the Emergency Department, with no other focal neurological sign in the examination. His clinical features were suggestive of the first presentation of a benign sexual headache, however complementary tests were made in order to rule out structural causes. Head CT scan, routine analysis, ekg, and chest x-ray were normal. After 8 hours, a LP was made, in order to rule out a SAH, with normal results. The study was completed with an EEG that showed no irregularities, and a MRI (DWI) demonstrated a small punctuate hyperintense lesion in the left hipoccampus. TTE, 24 h-holter monitoring and CADS were normal. Finally we conclude that he patient suffered a probable first episode of Headache associated with sexual activity (ICHD-III criteria), followed by an episode of Transient Global Amnesia (Hodges-Warlow criteria) with typical neuroimaging. Headache associated with sexual activity and Transient global amnesia are two entities related to sexual intercourse that neurologists must be familiar with, in order to rule out severe structural/organic processes, and then to inform patients about their benign prognosis.

PO195

Other primary headache disorders

Frontal thermography in healthy individuals and headache patients: reliability of the method

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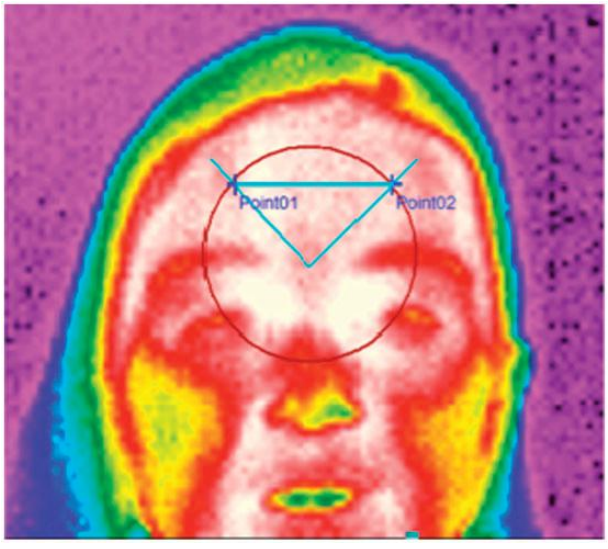
Introduction: Infrared Thermography detects infrared lights emitted by the body to visualize changes in temperature due to abnormalities in the surface blood flow of affected areas. This method may aid in the diagnostic process in pain medicine.

Objective: to assess the reliability of human body temperature measurement by means of Frontal Infrared Thermography (FIT).

Method: 35 volunteers with a mean age of 35 ± 11.6 years were evaluated. Fifteen out of 35 subjects were headache patients. FIT has been assessed with an infrared thermal camera (model LT3, Zhejiang Dali Technology Co. Ldt). The image analysis evaluated the temperature in two target points in the frontal polar sites. The measurements were performed in two separate sessions (T1 and T2), each session being the mean of three separate measurements. The Asymmetry Index, ANOVA 1 way, intra-class correlation coefficient and Pearson's correlation coefficient for the T1 were calculated. ANOVA 2 way compared the measurements between T1 and T2

Results: The analysis of variance did not show statistically significant difference between three consecutive measurements during the T1 and T2. The best reliability was found between the second and the third measurement. The statistical test ANOVA 2 way did not revealed intra-individual test-retest variations. The absolute value of the difference between temperature measured in the left and right side resulted to be different in healthy subjects and patients. No correlation was found between FIT and other clinical variables.

Conclusions: FIT can be considered an effective method for the temperature evaluation in controls and headache patients.



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Other primary headache disorders

Peripheral nerve stimulation as a treatment for drug-resistant cranial neuralgias

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Introduction: Cranial neuralgias are distinct, treatable syndromes which comprise one of the possible causes of facial pain. Although some prophylactic medications and techniques have been proposed as treatments, there are still many refractory patients and other therapeutic options are warranted. Peripheral nerve stimulation (PNS) has been proposed as a promising therapy for these patients.

Aim: The aim of this study is to evaluate the efficacy and tolerability of PNS for the treatment of refractory cranial neuralgias.

Material and Methods: Thirteen patients (4 men, 9 women, average age 52.5 ± 12.1) suffering from different drug-resistant cranial neuralgia were enrolled and implanted with a neurostimulation device. Five suffered from occipital neuralgia, 4 had postherpetic neuralgia and 4 had trigeminal neuralgia. The primary endpoint was the reduction in Analogical Visual Scale (AVS). Patient satisfaction, side effects and reasons for discontinuation were also studied. Significance level was set at $P < 0.05$.

Results: Pain severity according to the AVS was reduced from 8.9 ± 0.8 before PNS to 4.8 ± 2.6 after treatment initiation. 62% of treated patients were satisfied or very satisfied with the procedure. The most common adverse event was persistent implant site pain and three patients required to be explanted due to inefficacy. There were not differences between different subgroups.

Discusion: PNS has been explored as a possible treatment option in selective drug-resistant cranial neuralgias and, according to our results, this technique may be effective, safe and well tolerated in treating them. More studies are warranted to confirm these results.

PO197

Other primary headache disorders

Abnormal visual evoked potentials and photophobia in patients with migraine

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Background: Migraine is the most common neurologic disorder causing photophobia, which is one of the major diagnostic criteria for migraine according to the International Classification of Headache Disorders. Photophobia 'seems to be an intrinsic property of migraineurs". And it has been postulated that migraine is associated with 'visual pathway dysfunction" from retina to occipital lobes.

Aim: To assess the relationship between photophobia and abnormal pattern reversal visual evoked potentials (PR-VEP) in patients with migraine.

Method: 38 Patients with migraine [5 male, 33 female, 29 migraine with photophobia, 9 migraine without photophobia] were recruited according to international headache society classification from Madras institute of neurology, India and were subjected to PR-VEP. P100 latency is considered to be abnormal if >110 milliseconds. Relationship between abnormal P100 latency and photophobia in patients with migraine is assessed.

Results: P100 latency is significantly abnormal in patients with migraine and photophobia (p value 0.001 on right side and 0.003 on left side).

Conclusion: P100 latency is significantly abnormal in migraineurs with photophobia.

Keywords: Migraine, Pattern Reversal Visual Evoked Potentials

PO198

Other primary headache disorders

Idiopathic intracranial hypertension – comorbidities preceding diagnosis

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Background: Idiopathic intracranial hypertension (IIH) mainly affects young obese women. Aetiology of IIH is incompletely understood. Some medications and disorders such as hormonal disturbances, anemia and coagulopathy have been reported more frequently among IIH patients. However, results are inconclusive.

Aim: To investigate pharmacological treatments and comorbidity before diagnosis of IIH.

Method: The Swedish Patient Register identified 124 patients with a diagnosis of IIH (ICD-10 code G93.2) at Karolinska University Hospital during 2006–2013. We reviewed the medical records to validate the diagnosis and collect information on possible risk factors such as pharmacological treatments and comorbidity before diagnosis of IIH.

Results: Totally 95 patients (77%) had a correct diagnosis and were included in the study. Excluded patients received diagnosis by mistake, initial suspicion or incomplete investigation. The female/male ratio was 5,3:1. Males were older at the time of diagnosis, 60% where $\geq$40 years old compared with 17% among females. 11% were exposed to tetracyclines and 7% to corticosteroids in the year preceding diagnosis of IIH (all females). 8% of females had a diagnosis of polycystic ovary syndrome and 4% were diagnosed with IIH during pregnancy/postpartum. Among males 20% had obstructive sleep apnea syndrome. Disease affecting hormonal systems was reported in 12% of the patients, diabetes in 5%, kidney disease in 5%, coagulation disease in 2% and anemia in 3%.

Conclusion: This study showed that tetracyclines and corticosteroids could be associated with IIH among females. The observed comorbidities are mostly associated with hormonal imbalance and obesity.

PO199

Other primary headache disorders

Occipital nerve stimulation – first Czech experiences

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Introduction: Occipital nerve stimulation (ONS) has been demonstrated to be effective in the treatment of refractory headache, usually in the following three groups: chronic migraine, cluster headache and occipital neuralgia. Transcutaneous nerve stimulation (TENS) in the occipital region operates in a similar manner as the implanted occipital stimulator. The positive TENS result can predict good effect of chronic stimulation in 90%.

Methods: We present our first experience with ONS in 16 patients with refractory headache (chronic migraine. 8 patients, cluster headache: 2 patients, occipital neuralgia: 6 patients) in years 2011–2014. All patients underwent TENS in the standard localisation for at least 1 month. The effect of stimulation was estimated percentually, by visual analogue scale (VAS) and by other tests (MIDAS, HIT-6 and PDI). 11 patients were implanted with permanent subcutaneous stimulator.

Results: Number of TENS responders (improvement of at least 50%) amounted to 81.3%, with an average improvement of 62.5%. We observed a significant decrease in the intensity and frequency of headache and its impact on quality of life. The average score values decreased for HIT-6 by 14 points, PDI 15 points and MIDAS even by 31 points. The visual analogue scale pain intensity decreased on average from 8 to 5. The effect was similar for all types of pain. More prolonged TENS was limited by transient skin reactions in the area of electrodes. Improvements in the subsequent chronic stimulation varies between 50–90%.

Conclusion: Occipital nerve stimulation is effective non-pharmacological treatment of a broader range of refractory headaches.

PO200

POST-TRAUMATIC HEADACHE

Characteristics of posttraumatic headache following mild traumatic brain injury in military personnel in Iran

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Aims: The primary goal of this study was to evaluate the incidence and characteristics of posttraumatic headache attributed to mild brain injury in military personnel in Iran within a prospective and observational study design.

Methods: A prospective observational study was conducted with a cohort of military personnel under military education during a 6- month period at the Military Education Center in Isfahan in Iran. 322 military personnel under education were selected randomly and were given a 13-item mild brain injury questionnaire accompanied with affective disorders and headache questionnaires and were reevaluated after a 3-month interval.

Results: A total of 30 (9.3%) of the 322 military personnel met criteria for a mild brain injury. Among them, 18 personnel (60%) reported having headaches during the 3-month reevaluation. Posttraumatic headaches (PTH) defined as headaches beginning within 1 week after a head trauma were present in 5.6% of military personnel under study during 6 months. In total, 67% of PTHs were classified as migrainous or possible migrainous features. Patients with affective disorders such as PTSD and depression were at a higher risk for developing PTH following mild brain injury ($p < 0.05$). PTH did not relate to demographic factors such as age or type of trauma.

Conclusions: PTH attributed to mild brain injury is a common disorder in military personnel. Migrainous features are predominant among them in comparison with the general population. PTH is not related to a type of trauma, but has association with affective disorders.

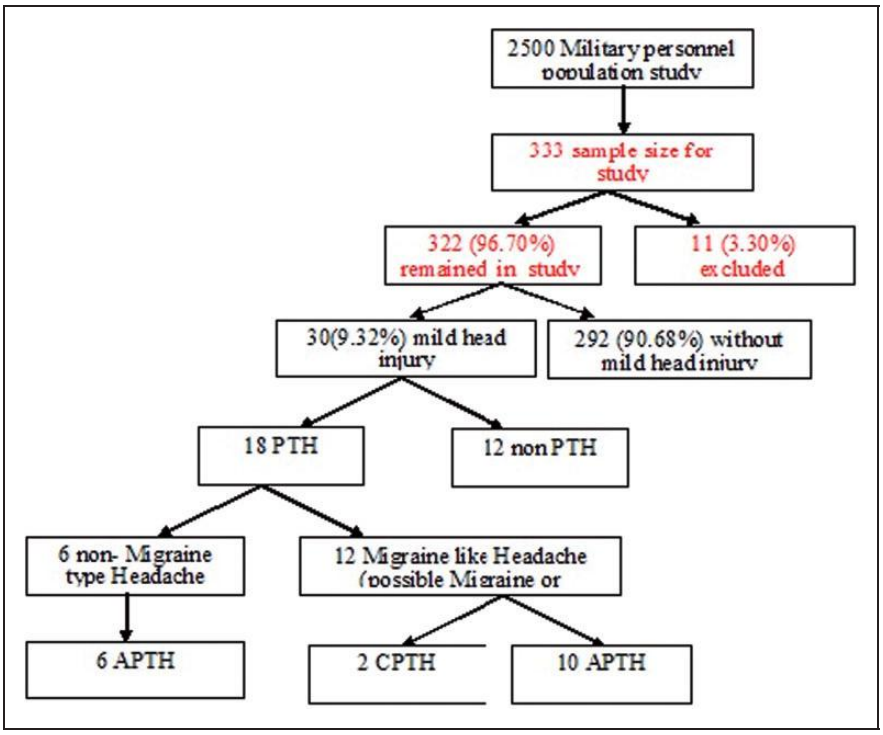

Figure 1. Study flow chart

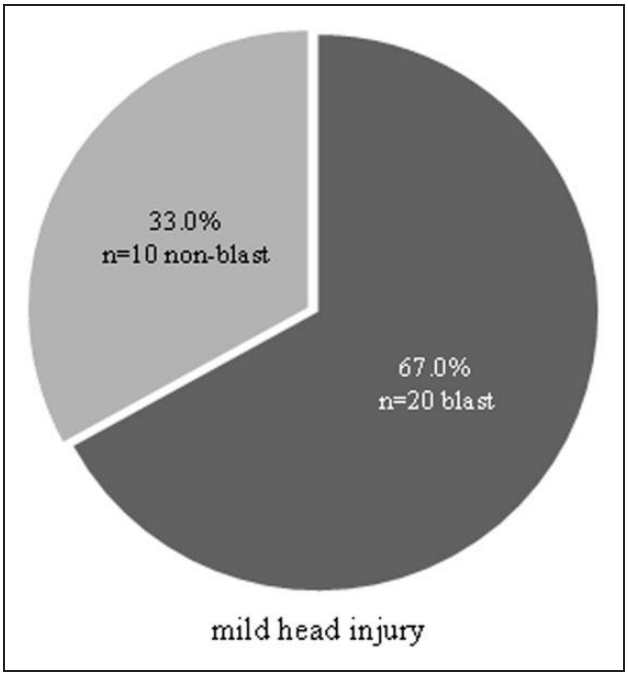

Figure 2. Mechanism of mild brain injury n = 30 out of 322 sample size.

PO201

POST-TRAUMATIC HEADACHE

Relación entre la articulación temporomandibular, articulación atlantoaxoidea y cervicalgias

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Summary: The title of this article and the reason for it are to be found in the controversial who means the diagnosis of the union of the following symptoms: vertigo, headache, earache, noise in the temporomandibular joint (TMJ) joint, cervical spine pain and upper back pain, feeling of ears covered. Through a tour of embryology, anatomy and function, is an integral vision of the buccal organ in order to highlight their influence on the development of skull, face and neck. One gets to demonstrate the relationship between dysfunction of the TMJ and the dysfunction of the atlantoaxoidea-occipital joint and the aforementioned symptoms. This relationship is common in clinical practice, although in most cases it is not diagnosed as such,

therefore the time and cost of treatment is increased with loss of money for the patient or for the State. In order to facilitate the diagnosis, through clinical cases show courts and lines that form the Araque Protocol, which allows a quick visualization of the problem. At the same time contributing to schedule a simultaneous multidisciplinary treatment that allows the rapid positive evolution of the patient. The study of 60 clinical cases (Avila Clinic and Hospital Pediatric Elias Toro) showed anatomical and functional changes with pain reduction in 95% of the clinical cases studied.

Keywords: 1. Functional Orthopedics – 2. Function – 3. Atlantoaxoidea-Occipital Joint. – 4. Temporomandibular Joint. – 5. Pain

PO202

POST-TRAUMATIC HEADACHE

Associations between headache and previous traumatic head injuries: a historical cohort study (HUNT)

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Background: Headache attributed to traumatic head injury is stated to be among the most common secondary headache disorders, yet the available epidemiological evidence is scarce.

Aim: To investigate whether the prevalence of headache was higher among individuals previously exposed to head injury compared to an uninjured control group.

Methods: This is a population-based historical cohort study. Data from hospital records on previous exposure to head trauma were linked to a large epidemiological survey (The Nord-Trøndelag Health Survey, HUNT 3) with validated data on headache occurrence. Participants without head trauma according to hospital records were used as controls. The head injuries were classified according to the Head Injury Severity Scale (HISS) and the International Classification of Headache Disorders (ICHD-3 beta).

Binary logistic regression was performed to investigate the association between headache and trauma, controlling for age, gender, anxiety, depression and socioeconomic status.

Participants in HUNT 3 have signed a written informed consent.

Results: The exposed group consisted of 940 individuals and the control group of 38,751 individuals. There were significant associations between trauma and any headache (OR 1.19, 95% CI 1.04 – 1.37), migraine (OR 1.47, 95% CI 1.20 – 1.79), chronic daily headache (OR 1.87, 95% CI 1.37 – 2.61), and medication overuse headache (OR 2.10, 95% CI 1.34 – 3.28). This was evident only for those with mild head injury. Multiple traumas were more strongly associated with headache.

Conclusions: The occurrence of headache was higher among individuals earlier exposed to a traumatic head injury compared to uninjured controls.

PO203

POST-TRAUMATIC HEADACHE

QEEG abnormalities in posttraumatic headaches in forensic sample

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Objectives: The aim of the investigation is to contribute to electrophysiological characterization of the subjects with posttraumatic headaches.

Methods: The resting EEG activity and LORETA for the EEG spectral beta band were evaluated in 24 subjects, 14 with and 10 without posttraumatic headaches. All subjects were assessed using the CIE- criteria. The EEG visual inspection characteristics and the use of frequency domain quantitative analysis techniques (Narrow band spectral parameters) are described.

Results: QEEG analysis showed a pattern of excess of beta activity on the left frontal regions in the posttraumatic headaches group. LORETA signified an increase of beta activity (14.84 Hz) in experimental group within left fronto-temporo-limbic regions.

Conclusions: The beta power increase may also be reflecting abnormally enhanced cortical excitation in patients with this pathology.

PO204

POST-TRAUMATIC HEADACHE

Physiotherapy in the treatment of disturbances of autoregulation of cerebral circulation in patients with post-traumatic headaches

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In the mechanism of developing headache in traumatic brain injury neurodynamic shifts caused by disturbances of cerebral hemo – and liquor-dynamics play an important role.

The aim of our study was to determine the effect of physiotherapy on the autoregulation of cerebral circulation in patients with consequences of TBI.

Method: We observed 65 patients with consequences of mild traumatic brain injury. All patients were examined by Doppler ultrasound. Patients were divided into two groups: the first group were patients who received standard therapy. The second group included patients who received standard therapy and in addition physiotherapy using the method of magnetic therapy and darsonvalization.

Results: In the first group we observed changes in the form of increased linear velocity of blood flow (BFV) to $0{,}34 \pm 0{,}05$ before treatment and $0{,}35 \pm 0{,}03$ after treatment. RI before treatment was $0{,}96 \pm 0{,}04$ and $0{,}93 \pm 0{,}05$ after treatment. PI before treatment was $1{,}75 \pm 0{,}02$ and $1{,}66 \pm 0{,}04$ after treatment. In the second group we observed increase in linear BFV to $0{,}32 \pm 0{,}02$ before treatment and $0{,}40 \pm 0{,}05$ after treatment. RI before treatment was $0{,}98 \pm 0{,}04$ and $0{,}87 \pm 0{,}03$ after treatment. PI was before treatment $1{,}73 \pm 0{,}02$ and $1{,}20 \pm 0{,}04$ after treatment.

Conclusion: The use of physiotherapy treatment in patients with consequences of traumatic brain injury leads to normalization of autoregulation of cerebral circulation by increasing the linear velocity of blood flow in the carotid arteries and decreasing of resistance indexes.

PO206

POST-TRAUMATIC HEADACHE

The influence of pre-injury headaches on outcome following concussion in children

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Headache is one of the commonest and most disabling features of post-concussion syndrome. As migraine often presents in childhood, the overlap of these two conditions and their influence on outcome is likely to be significant.

Objectives: To describe the characteristics of **pre-injury headaches** in children with concussion, and examine their influence on outcome.

Methods: Prospective study of children, aged 2–18yrs, presenting to ED. A standard questionnaire was used documenting the injury, previous headaches and family history. Outcome measure: Post-concussion symptom inventory at 1, 2 and 3 months post-injury. Logistic regression was used to predict outcome.

Results: 427 children (62% male; Age: 11.0yrs SD4.4yrs) participated in the study. 120 participants (21%) experienced pre-injury headaches, not diagnosed as migraine. 49 others had diagnosed migraine. Children with headaches were older ($p < 0.001$). Males were overrepresented in the previous migraine group (75%, $p = 0.05$). The headache characteristics in these groups are shown in Table 1.

56% of participants had >3 migraine features (probable migraine). 25% of children are had pre-injury migraines or "probable migraine". Although gender, previous headaches and migraine were not related to outcome, age and "migraine + probable migraine" strongly predicted outcome at 1 and 2-months post-injury (Pseudo R^2 0.06, $\chi^2(416) = 14.4$, $p < 0.001$).

Table 1. Headache characteristics

	Pre-injury Headaches	Pre-injury Migraine	
Pulsatile	78.5%	89.1%	$p = 0.107$
Photophobia	60.7%	95.9%	$p < 0.001$
Nausea	24.7%	55.1%	$p < 0.001$
Disabling	38.1%	83.3%	$p = 0.001$
Migraine 1o relative	34.9%	59.2%	$p = 0.037$

Conclusion: Careful categorization of pre-injury headaches helps to predict short-term outcomes.

PO207

POST-TRAUMATIC HEADACHE

Headache following surgical treatment of traumatic intracranial hematoma

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Introduction: Traumatic intracranial hematoma (TIH) represents a challenge for neurosurgeons due to its high mortality and morbidity rates. The most common complication of traumatic brain injury is posttraumatic headache. Only a few studies have discussed the headache from the standpoint of the result of surgical treatment of TIH.

Aim: In our study, the clinical data of patients with TIH, who underwent surgical treatment, were analyzed to determine: how often headache occurred in postoperative period of TIH and which factors are associated with headache following surgical treatment of TIH.

Methods: A total of 132 patients (mean age 43.4 ± 15.7 years, male/female ratio 3.8:1, median admission GCS score 8.5 ± 2.8), who underwent surgical removal of TIH, were included in this study.

Results: Follow-up neurological examination showed that, in 85 patients (64.3%) headache occurred after surgical removal of TIH. Factors associated with postsurgical headache were: significance of primary and secondary brain damage, volume of intracranial hematoma, midline shift and timing of surgery ($p < 0.01$). Disability rate in patients with headache was significantly higher compared to the patients without it (61.7% vs. 34.1%, $p < 0.01$).

Conclusion: Headache occurred in 64.3% cases after surgical removal of TIH. Factors associated with headache following surgical removal of TIH are: significance of primary and secondary brain damage, volume of intracranial hematoma, midline shift and timing of surgery. Postsurgical headache significantly negative affects the outcome of patients with TIH.

PO208

POST-TRAUMATIC HEADACHE

Post-traumatic headache can be physiologically discriminated from migraine with aura

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Apart from a chronological link to prior trauma, post-traumatic headache (PTH) is often clinically indistinguishable from other headache disorders. However, changes in autonomic regulation have been shown in several headache types and may serve as a basis for physiological distinction. Aim: Measure discrete craniofacial autonomic parameters, beginning with pupil function, and correlate with photophobia thresholds in post-traumatic and primary headache subgroups.

Five episodic PTH subjects were compared to age-matched non-headache (NH, $n = 11$) and migraine with aura (MA, $n = 8$). Classifications were made using the International Classification of Headache Disorders II criteria. *Photophobia thresholds (PPT) with dynamic pupillometry* were performed using a rheostat-modulated halogen light and infrared camera. *Pupil cycle time* (PCT) was recorded using a slit lamp. Groups were compared using Kruskal-Wallis test, followed by post-hoc pair-wise comparison.

PPT, pupillary light response (%-change from baseline to maximum constriction at PPT) and PCT were significantly different between all groups for all modalities. While PPT threshold did not differ significantly in PTH compared to other subgroups, the amplitude of pupillary constriction at PPT was significantly less. PCT was significantly longer in PTH compared to all groups.

PTH subjects differ significantly from NH and MA on autonomically mediated pupillary measures. The findings suggest a possible parasympathetic lesion in pupillary function versus persistently over-riding sympathetic drive. Future studies are needed to confirm this observation and ascertain whether this finding is limited to pupillary control, or if it represents a more widespread autonomic disturbance. Such differences may provide mechanistic insight into both diagnosis and treatment.

PO209

Other secondary headache disorders

Prevalence of venous sinus stenosis in pseudotumor cereberi (PTC) using digital subtraction angiography (DSA)

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Objectives: To Study the prevalence of intracranial venous stenosis in Pseudotumor cereberi patients.

Patients and Methods: Thirty patients diagnosed as PTC according to Dandy criteria. All underwent general and neurological assessment. Radiological assessment included CT scan brain +/– MRI brain without contrast, MRV. All underwent digital subtraction cerebral Angiography (DSA) (venous phase) to confirm the validity of filing gaps seen at the level of MRV.

Results: MRV brain showed that 24 patients (80%) showed filling gaps. Digital subtraction cerebral angiography (venous phase) showed 9 patients (30%) had stenosis in their dural sinuses. MRV showed to be a good screening tool since it had 100% sensitivity and negative predictive value. However, since it has a moderate specificity (62%) with a positive predictive value (PPV) of only 35%, then lesions detected should be confirmed with digital subtraction cerebral angiography (venous phase) particularly those involving the transverse and sigmoid sinus.

Conclusion: Studying the intracranial venous system in patients with PTC is an important step in understanding the pathophysiology of the disease. Detection of venous sinus stenosis opens the way to a novel therapeutic option for refractory patients like venous sinus stenting.

Keywords: Pseudotumor cereberi, venous sinus stenosis, headache, MRV, Digital subtraction angiography (venous phase).

PO210

Other secondary headache disorders

Clinical and radiological findings suggesting disorders other than tolosa-hunt syndrome among ophthalmoplegic patients: a retrospective analysis

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Background: Clinical presentations of Tolosa-Hunt syndrome (THS) are nonspecific and may overlap with many etiologies. Excluding other symptomatic painful ophthalmoplegias (SPOs) is essential for correct diagnosis.

Aim: To investigate clinical and radiological features of THS and examine their diagnostic value, and to propose clinical and radiological features that can discriminate SPOs from THS.

Method: Patients referred with painful ophthalmoplegia over 12 years were recruited retrospectively and allocated into THS or SPO groups. Typical symptoms and imaging of THS were proposed based on ICHD-3 beta criteria and previous literature. Atypical clinical and radiological features suggesting alternative diagnoses were also proposed to predict SPO. Initial presentations and imaging findings were registered and correlated with diagnostic outcomes. The predictive value of clinical and imaging findings was evaluated.

Results: Of the 61 referred cases, 25 were classified as THS and 36 as SPO. Nineteen of SPO cases (52.8%) manifested typical THS symptoms at onset. Patients with SPOs were prone to have atypical symptoms (47.2%) and radiographical findings (82.1%) compared to those with THS (4.0% and 4.2%, respectively; both $p < 0.001$). Both typical symptoms and imaging findings predicted a diagnosis of THS with high sensitivity (95.8% and 100%, respectively) but low specificity (47.2% and 28.6%, respectively). High sensitivity (82.1%) and specificity (95.8%) were achieved using atypical imaging features to predict SPO.

Conclusion: A diagnosis of THS based on clinical presentations or imaging results is not reliable. Identification of atypical imaging features may have a useful role in discriminating SPOs and thus avoid erroneous diagnoses.

PO211

Other secondary headache disorders

Neurogenic pruritus: response to low dose levetiracetam. Report of four cases

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Background: Neurogenic pruritus is not well known and its treatment is varied. We present three cases treated with low dose levetiracetam and excellent clinical response.

Cas1 1: 70 y/o female with a herpes zoster in T5. Acyclovir treatment was successful but she developed post-herpetic neuralgia with intense pruritus on the borders of the painful zone. Pregabalin improved only the pain. Topic treatments gave temporary relief. Levetiracetam, 250 mg at night abolished the pruritus in 48 hours. She is on chronic treatment with both medications.

Case 2: 75 y/o female with diagnosis of generalized anxiety who develops pruriginous skin lesions. No precise dermatologic diagnosis. After remission of the lesions she complains of pruritus in 'stocking' distribution. Local treatments and hydroxicine were ineffective. Levetiracetam, 250 mg at night improved pruritus by 70%.

Case 3: 25 y/o female with intercostal neuralgia treated with T10 rhizotomy somewhere else. Continuous neuralgic pain treated with many medications including opioids. She developed intense and continuous pruritus on the borders of the painful zone. Levetiracetam, 250 mg at night abolished the itch with no effect on pain.

Case 4: 80 y/o male with moderate Alzheimer's disease who had a V1 herpes zoster. After treatment with acyclovir, he complained of post-herpetic neuralgic pain and pruritus on the borders of the painful zone. Levetiracetam, 250 mg at night abolished the pruritus.

Discussion: Our series suggests that gabaergic receptors play a role in this condition. As far as we know, this is the first reported series on this matter. Neurogenic pruritus is underreported.

PO212

Other secondary headache disorders

Paroxetin vs amitriptilin: curative effect on depression and cardiac side effects in eldery women with chronic tension-type headache

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Background: It is well documented that depression is associated with headache and the prevalence of secondary headache disorders increases in the elderly. There is limited knowledge regarding the relation between recurrent primary headaches and depression symptoms of among eldery women.

Methods: Fifty-eight female patients 65–85 y.o (28 Amitriptilin (50 mg), 30 Paroxetin (20 mg) group) with depression secondary to chronic tension-type headache (TTH) were enrolled in our study. All patients were without history of heart diseases. Patients were evaluated before and 3 months after the treatment.

Results: In both groups, the number of painful days in a month, visual analogue scale values and Hamilton depression score decreased after the treatment. As a result, all of the parameters were found to have improved in both groups ($p < 0.001$), the results were statistically significant. Transient ventricular repolarization disorders and paroxysmal arrythmia during treatment were significantly more frequent in the Amitriptilin group than in the Paroxetin group ($p < 0.001$).

Conclusions: Paroxetin is more safety than Amitriptilin in eldery women. Assessment of co-morbid disorders is important in order to improve the management of eldery with chronic TTH.

PO213

Other secondary headache disorders

Onabotulinumtoxina therapy for treatment of chronic daily headache secondary to meningeal traction

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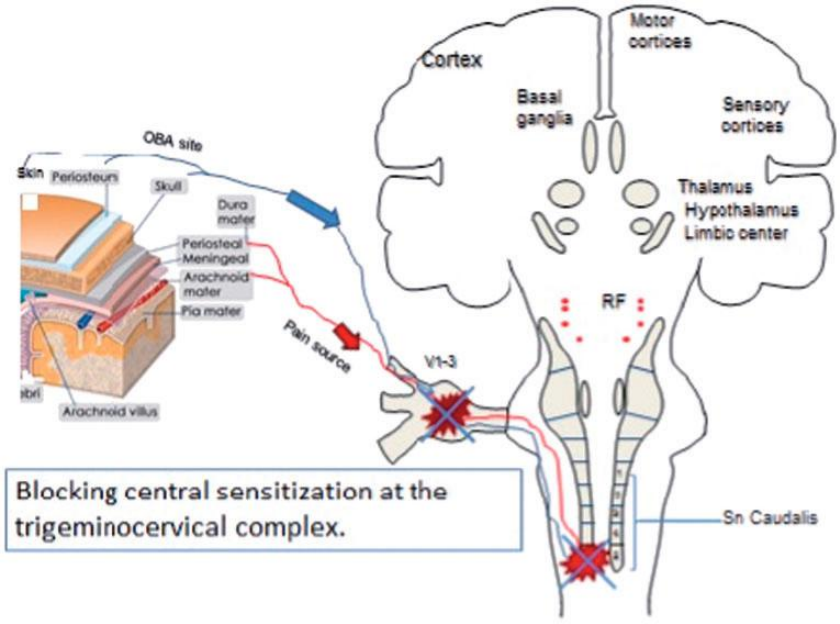
A 48-year-old man with a history of congenital non-communicating hydrocephalies—with multiple shunt revisions

and a recent shunt series without obstruction—presented to the neurology clinic for headache management.

MUSCLE	SIDE	# OF SITES & DOSE	TOTAL MUSCLE DOSE
Head			
Frontalis	Right	4 sites of 5 units each	20 units
Corrugator	Right	One site at 5 units	5 units
Temporalis	Right	2 sites at 10 units each	20 units
Occipitalis	Right	5 sites at 5 units each	25 units
Frontalis	Left	4 sites of 5 units each	20 units
Procerus / Corrugator	Left	One site at 5 units	5 units
Temporalis	Left	2 sites at 10 units each	20 units
Occipitalis	Left	1 site at 10 units each	10 units
Right Neck			
Sternocleidomastoid	Right		
Trapezius	Right		
Splenius / Semispinalis Capitus	Right	2 sites; 1 sup at 10 units & 1 inf at 5 units	15 units
Levator scapula	Right		
Scalene	Right		
Left Neck			
Sternocleidomastoid	Left		
Trapezius	Left		
Splenius / Semispinalis Capitus	Left	2 sites; 1 sup at 10 units & 1 inf at 5 units	15 units
Levator scapula	Left		
Scalene	Left		
Total Dose			155 units

since the ventriculoatrial shunt was placed (final revision). He continues to receive OBA every 3 months with good relief.

The patient continued to have episodes of meningeal traction secondary to intracranial hypertension and hypotension up till the final shunt revision. Inhibition of peripheral and, indirectly, central sensitization with OBA was achieved mechanistically by a decrease in neurogenic inflammation in the same fashion achieved with chronic migraine. What makes this patient's response unique is the postural nature of his headaches. OBA therapy, by acting on peripheral trigeminal pain fibers in the scalp, which also innervate the meninges, markedly reduced this patient's postural headaches (Figure 1).



Blocking central sensitization at the trigeminocervical complex.

Over the course of three year the patient had multiple shut revisions and a headache consistent with a transformed migraine secondary to alternating hypotension and hypertension. The patient was tried on multiple headache prophylaxis without significant relief. At which time a standard chronic migraine OnabotulinumtoxinA (OBA) treatment pattern (Table 1). Within 3 days of the injections, his chronic daily headache scores dropped to 0–1/10 from 5/10 and his postural sharp/throbbing headache decreased to one time a day, lasting only 20 to 30 minutes from multiple times a day lasting hours. The patients final shunt revision was done 4 months prior to his first OBA therapy and had not required further surgical intervention

PO214

Other secondary headache disorders

Headache associated with pituitary lesions: a longitudinal cohort study

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Patient characteristics

	All Patients n = 133	With regular Headache n = 84	Without regular headache n = 49	p-value
# Female (%)	86 (65%)	63 (75%)	23 (47%)	p = 0.001
Average Age	48	45	55	p = 0.0003
Average BMI	28.96	28.54	29.69	p = 0.3075
Prior Migraine or Headache Diagnosis	44/132 (33%)	39/83 (47%)	5/49 (10%)	p < 0.0001

Aim: To characterize headache in patients referred to a neuroendocrine clinic with suspected pituitary lesions and to assess changes in headache in those who underwent surgery.

Methods: We used a self-administered survey of headache characteristics in patients upon presentation and following any pituitary surgical procedure.

Results: 133 participants completed the questionnaire (response rate of 99%). The prevalence of headache was 63%. Compared with patients without headache, the group with headache was more likely to be female (p = 0.001), younger (p = 0.0003), and have a prior headache diagnosis (p < 0.0001). 71.9% of subjects reported headache localized to the anterior head. 26 patients with headache underwent transsphenoidal pituitary surgery. Headache was not associated with increased odds of surgery (OR 0.82). At three months, 80.8% of surgical patients reported improvement or resolution of headaches. No patients developed new post-surgical headache.

Conclusions: Frequent, disabling headaches are common in patients with pituitary lesions referred for neuroendocrine consultation, especially in younger females with a pre-existing headache disorder. Surgery was frequently associated with headache improvement or resolution and did not cause or worsen headaches. The International Classification of Headache Disorders diagnostic criteria should be revised to better reflect these and other research findings.

PO215

Other secondary headache disorders

Headache improvement after treating patients with aneurysmal subarachnoid hemorrhage

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Purpose: The purpose ofthis study was to evaluate headache in patients who had been treated for aneurysmalsubarachnoid hemorrhage (aSAH) and to investigate its predisposing factors.

Materials and Methods: A total of217 patients were included. The included patients had to be alertwith moderate-to-severe headache. Other inclusion criteria included thepresence of a ruptured intracranial aneurysm, good clinical outcome atdischarge, and at least one year of follow-up clinical and radiographic data(including visual analog scale [VAS] scores). We studied the changes in VASscores from initial to follow-up in order to investigate the predisposingfactors of VAS changes.

Results: One-hundredeighty-two (83.9%) patients experienced improvement in VAS score $\leq$3 upon discharge. The VAS score at discharge was significantly lower than thaton admission ($P < 0.001$). The independent predisposing factors for headacheimprovement were previous stroke,previous headache treated with medication, and endovascular treatment (EVT). EVT and symptomatic vasospasmwere independently associated with VAS decrement through the follow-up period.

Conclusion: Patients with aSAHwho initially had moderate-to-severe headache experienced significant headacheimprovement at discharge, with continuously decreasing VAS scores over 12months of follow-up. Headache improvement might be expected in patients whowere treated with EVT or in those who do not have a history of headache(treated with medication) or of stroke. After discharge, continuous decreasesin the VAS score might be expected in patients who were treated with EVT or intthose who did not experience symptomatic vasospasm.

PO216

Other secondary headache disorders

Treatment and prognosis of subdural hematoma in patients with spontaneous intracranial hypotension

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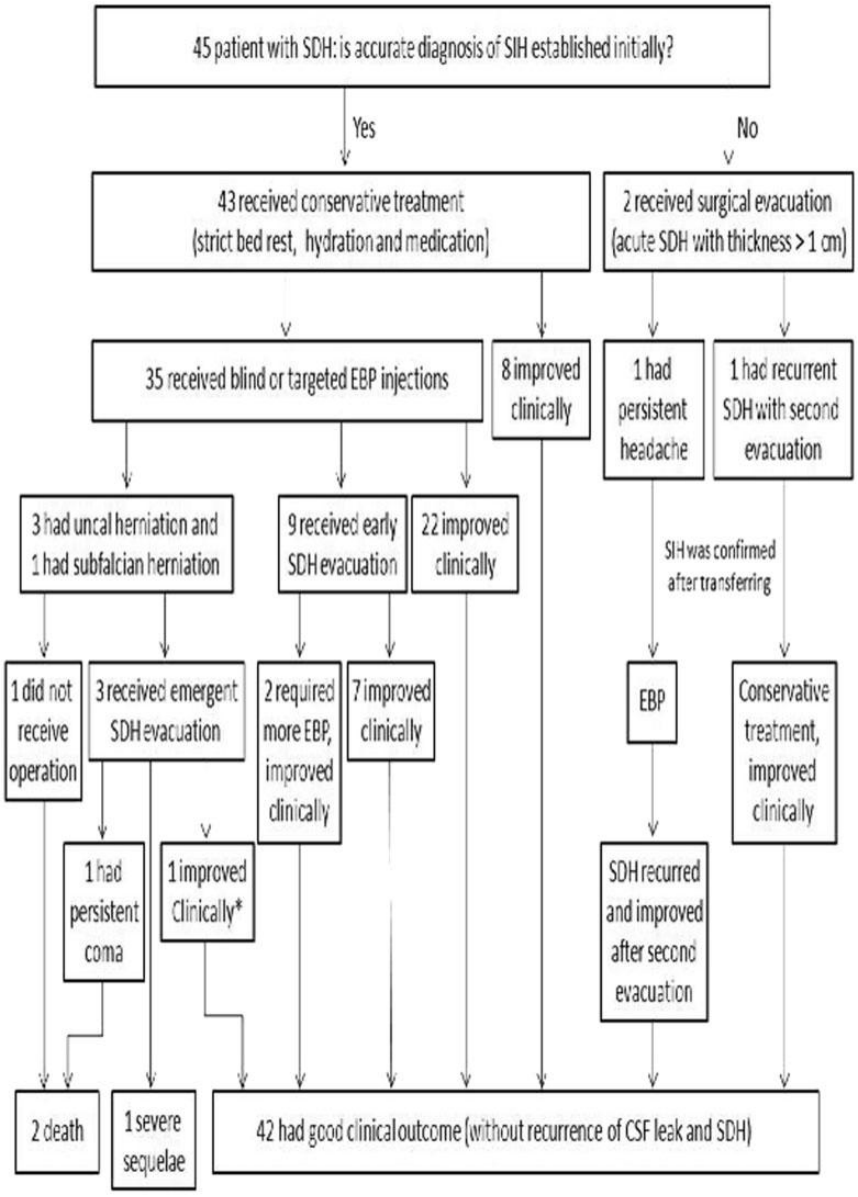

Objective: To elucidate the outcome, prognostic predictors and timing of surgical intervention for subdural hematoma (SDH) in patients with spontaneous intracranial hypotension (SIH).

Methods: Patients with SDH were identified retrospectively from 227 consecutive SIH patients at four hospitals. Data were collected on demographics, clinical courses, neuroimaging findings, and treatment of SDH, which was later divided into conservative treatment, epidural blood patches (EBP), and surgical intervention. Poor outcome was defined as severe neurological sequelae or death.

Results: Forty-five patients (20%) with SDH (mean maximal thickness 11.9 ± 6.2 mm) were recruited. All 15 patients with SDH

Conclusions: Uncal herniation results in poor outcomes in patients with SIH complicated with SDH. In individuals with SDH ≥ 10 mm and decreased GCS scores, early surgical evacuation might prevent uncal herniation.

PO217

Other secondary headache disorders

Essential thrombocythaemia with JAK2 mutation and its relationship to benign intracranial hypertension as a cause of secondary headache

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Background: Essential thrombocythaemia has been well described in the literature to cause neurological complications because of increased risk of thrombotic events. However, very few cases have described the atypical presentation of benign intracranial hypertension, in the absence of intracranial thrombotic events, on the background of essential thrombocythaemia.

Aim: This will be the first reported case in South Africa of atypical benign intracranial hypertension and its association with essential thrombocythaemia. The last reported case was in 1989 in the UK; however, a more convincing case presentation will be presented to demonstrate the existence of this clinical phenomenon.

Method: Analysis of haematological, radiological and genetic studies will be discussed. Further analysis of the literature will be done and arguments will be created both for and against the existence of such a relationship and possible pathophysiological mechanisms that may play a role in the development of benign intracranial hypertension with a background of essential thrombocythaemia.

Results: Taking into account the related literature and case reports similar to our case, an opinion is drawn that a relationship between benign intracranial hypertension and essential thrombocythaemia does exist.

PO218

Other secondary headache disorders

Early botulinum toxin injection relieves trigeminal neuropathic pain after dental implant surgery

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Introduction: Although botulinum toxin type A (BoNT-A) may induce antinociceptive effects, behavioral evidence for the antinociceptive effects of BoNT-A on orofacial neuropathic pain has not been reported previously.

Aims: In this present study, we investigated the antinociceptive effects of BoNT-A in rats with trigeminal neuropathic pain produced by mal-positioned dental implants (MDI).

Methods: Experiments were carried out with male Sprague-Dawley rats. Under anesthesia, the left mandibular second molar was extracted, followed by the placement of a miniature dental implant to induce injury to the inferior alveolar nerve. Mechanical allodynia was evaluated by the application of air-puff pressure on freely moving rats.

Results: MDI produced obvious nociceptive behavioral changes in the rats, including a significant reduction in the air-puff threshold on the ipsilateral side of the injured site. Subcutaneous injection of 1 or 3 U/kg BoNT-A attenuated mechanical allodynia significantly [$F_{(3,\ 28)} = 867.597$; $p < 0.001$]. In the group treated with 1 U/kg BoNT-A, the anti-allodynic effects persisted on postoperative Day 18. A single injection of 3 U/kg BoNT-A produced the prolonged anti-allodynic effects for the entire experimental period relative to the saline-treated group.

Conclusions: In summary, the results from this study suggest that BoNT-A injection can be used for treating trigeminal neuropathic pain after dental implant surgery.

PO219

Other secondary headache disorders

Characterization of japanese cases of reversible cerebral vasoconstriction syndrome (RCVS)

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Background and Purpose: Reversible cerebral vasoconstrictionsyndrome (RCVS) is characterized by

thunderclap headache and constriction ofcerebral arteries with or without focal neurological deficits and vascularevents such as intracranial hemorrhage, cortical subarachnoid hemorrhage (SAH), and/or cerebralinfarction.

Aim: To identify the clinical variations of domestic cases of RCVS and tocharacterize Japanese cases of RCVS patients, we examined the clinical featuresof nine RCVS patients

Method: Nine consecutive patients diagnosed as having RCVS from 2008 to2014 in our hospital were investigated. Their clinical features were documented,and MRI and MRA were performed at least twice for each patient to confirm both thepresence of cerebral vasoconstriction and recovery from vasoconstriction.

Results: There were seven females and two males with a median age of 46 years (27–53). All the patients experienced thunderclap headache. Five patients hadcerebrovascular complications: two had both cerebral hemorrhage and cortical SAH, one had intraparenchymal hemorrhage, one had bothcerebral infarction and cortical SAH, and one had cortical SAH. Seven patients were treated with verapamil. Their clinicalcourses were fairly benign; however, one patient had hemiparesis as a sequela. Inanother patient, RCVS was found to be associated with pheochromocytoma in herright adrenal gland which was surgically removed.

Conclusion: Japanese cases of RCVS show similarities to Caucasian casesreported in the literature in terms of clinical features, sex ratio, and ratioof cerebrovascular complications.

PO220

Other secondary headache disorders

A case of acute interhemispheric hemorrhage manifestating solely as a headache

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Case: 69-year-old woman in thoracic surgery consulted to department of neurology complaining of sudden onset of headache. She was recovering from coronary artery bypass graft surgery for weeks. The headache was continuous, dull-pulsating in quality and located in bilateral frontotemporal regions. At first she did not reported any traumatic event but close history taking revealed that she had slip down when rising from bed with bumping head to the wall in hospital room. Her physical examination showed no significant abnormalities. Other cranial nerves were within normal limits. Computed tomography(CT) scan revealed a high density lesion in the left medial frontal area with no contrast enhancement, suggestive acute parafalacian SDH. She was medically conservative treated. One week later the follow up CT showed complete remission of subdural hemorrhage.

Discussion: The most common cause of ISH is usually by traumatic laceration of bridging veins between the parietooccipital cortex and the superior sagital sinus. Other causes of ISH are intracranial aneurismal rupture, surgery in and around the corpus callosum. Here in the case, specific traumatic lesion wasn't to be found. The diagnosis of ISH is mainly based on the CT. The treatment guidelines are unclear, and both conservative and surgical management have been equally advocated. Even though ISH is a rare event, it should be considered among the diagnostic possibilities in elderly patients who present with headache as the sole symptom without other clinical features. Also since a minor trauma could cause acute ISH, a careful and detail history taking is indispensable.

PO221

Other secondary headache disorders

Neck tongue syndrome: a systematic review

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Background/Aim: Neck-Tongue Syndrome is characterized by brief attacks of neck and/or occipital pain accompanied by abnormal sensation or posture of the ipsilateral tongue. Attacks are brought out by head turning and thought to represent lateral atlantoaxial joint subluxation compressing the C2 ganglion, which receives afferent input from the lingual nerve. We undertook this systematic review to understand better this rare disorder.

Methods: We searched PubMed and ScienceDirect for "neck-tongue syndrome" and reviewed all English language references. We reviewed conference proceedings from recent headache meetings, and report two new cases. Cases were abstracted using a standardized form and classified as primary if episodic and brought out with head turning, or secondary if symptoms were persistent. Demographic and clinical features of primary cases were analyzed.

Results: There were 34 primary cases; 53% female. Mean age (SD) at onset was 13.3 (6.9) years. Nineteen (56%) experienced neck pain, 5 (15%) occipital pain, and 10 (29%) both. Pain was most often sharp or stabbing and

severe, lasting several seconds to several minutes. Eight experienced numbness/tingling in the neck/occiput following the pain. Thirty-one had an accompanying tongue sensory disturbance and three a motor/posture disturbance; five had both. Nine had other headaches, and four a family history of neck tongue syndrome.

Conclusions: Neck-Tongue syndrome (NTS) typically has pediatric onset, suggesting ligamentous laxity during growth and development facilitating transient subluxation of the atlantoaxial joint with sudden head turning. Familial cases suggest a genetic predisposition in some individuals. NTS should be re-instated to ICHD-III.

PO222

Other secondary headache disorders

Loss of periventricular white matter structural integrity in patients with idiopathic intracranial hypertension

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Background: periventricular white matter hyperintensities (PVH) have been found in hydrocephalus. Whether there are changes in WM structure of patients with idiopathic intracranial hypertension (IIH) is unknown.

Objectives: To evaluate the macro/microstructural WM integrity in patients with IIH.

Methods: In this prospective study we recruited 14 consecutive patients (1 men and 13 women, mean age 41 years, SD 14; mean BMI = 32, SD = 5), who fulfilled the diagnostic criteria for IIH with and without papilledema, as well as 14 patients with chronic or recurrent migraine, matched for sex and age. All subjects underwent neuroimaging studies including 3-tesla MRI and 3D-PC MR venography of the brain, while fractional anisotropy (FA) and mean diffusivity (MD) values were obtained from diffusion tensor imaging (DTI) scans. Results were correlated with CSF opening pressure, mean and peak CSF pressure, abnormal pressure waves.

Results: 3 T MR imaging study of the brain found periventricular WM hyperintensities more frequently in patients with IIH (79%) than in patients with primary headache disorders (35%). While, the voxel-based analyses of DTI images revealed a significant increase of mean diffusivity values in the periventricular area of posterior horns in patients with IIH ($MD = 0.0030 \pm 0.0003$, IIH; $MD = 0.0024 \pm 0.0003$, Migraine; $p < 0.002$). Structural alterations in the periventricular WM were related with peak CSF pressure and abnormal pressure waves.

Conclusions: We found CSF pressure-related structural WM alterations in patients with increased intracranial pressure, suggesting a loss of WM structure integrity in IIH.

PO223

Other secondary headache disorders

Obesity-related intracranial hypertension in the rat – a possible idiopathic intracranial hypertension (IIH) model?

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Background: Idiopathic intracranial hypertension (IIH) is a condition of increased intracranial pressure (ICP) without identifiable cause. The majority of IIH patients are obese, which suggests a connection between CSF regulation and obesity. However, the pathophysiological mechanisms remain widely unresolved.

Aim: To develop a long-term ICP monitoring method and investigate ICP in lean and obese rats. We also aimed to clarify if any ICP difference could be attributed to changes in some well-known ICP modulators; retinol and arterial partial pressure of CO_2 (pCO_2).

Methods: ICP was measured in six obese and six lean Zucker rats with a newly developed epidural ICP monitoring method over a period of 31 days. Furthermore, arterial pCO_2 and serum retinol were measured in blood samples from each animal.

Results: Obese rats had significantly elevated ICP-levels compared to lean controls on all recording days ($p < 0.0001$). Serum retinol (lean: 10.54 ± 0.36, obese: 11.70 ± 0.91, $p = 0.35$) and arterial pCO_2 (lean:

37.17 ± 1.58, obese: 41.25 ± 1.80, p = 0.16) did not differ between the two groups.

Conclusion: Obesity-related intracranial hypertension in rats is not related to altered pCO_2 levels or retinol metabolism. This indicates that the increase in ICP might be related to molecular changes in the brain caused by the adipose state. Although further studies are warranted, obese Zucker rats could potentially constitute a model for IIH.

PO224

Other secondary headache disorders

A patient with symptomatic migraine due to cerebral arteriovenous malformation

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Background: Headache has been reported to be the presenting symptom in relatively few patients with cerebral arteriovenous malformation (AVM). It can imitate various primary headaches but most often takes the form of migraine.

Case report: 26-year old female was admited to neurologic department after second episode of 20 minutes lasting scintillating vision disturbance in left eye and left-sided paresthesia with concomitant right sided pulsating headache and nausea. Brain MRI revealed 3 cm large AVM in right parietotemporal lobe. DSA showed that main feeders were branches of right posterior cerebral artery and right middle cerebral artery, the venous drainage was through cortical veins to superior saggital sinus. After evaluation of bleeding risk and risk of invasive treatment complications the decision for endovascular treatment was accepted. Six months after presenting symptoms endovascular treatment with embolisation was conducted, the complete exclusion of AVM was achieved. After treatment headaches disappeared.

Discussion: Patient had suffered several episodes of typical migraine with aura. Contralateral headache compared to aura symptoms was a red flag, which dictated imaging diagnostic. AVM in right parietotemporal lobe was revealed. Etiological connection betwen AVM and migraine was proposed and finnaly proved with disappearence of headaches after AVM exclusion.

AVM exclusion is intended to prevent bleeding, which is the most dangerous complication. When the risk of AVM treatment exceeds the risk of spontaneus bleeding, the conservative approach is reasonable.

Conclusion: AVM may present as migraine like headache. There is a favourable impact on headache by removal of AVM.

PO225

Other secondary headache disorders

An unusual presentation of neurosyphilis as a probable migraine

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Backround: Syphilis has reappeared as a worldwide problem. Use of antibiotics has modified the forms and stages of syphilis and, subsequently, the clinical features of neurosyphilis. Headache, although rare, is part of neurosyphilis. We describe a case that initially presented as refractory migraine, which was subsequently diagnosed as neurosyphilis.

Case presentation: A 38-year-old sailor had a 6 years history of sustained diffuse headache located primarily at the frontal region. The neurological examination and brain imaging were normal and the symptoms were attributed to stress. He was treated with antidepressants, with no clinical response. The headaches gradually worsened and acquired the characteristics of migraine, without aura. Six years after the initiation of the headache the patient was admitted in the hospital presenting a severe episode of probable migraine with vertigo. He was submitted to a thorough imaging and neurophysiologic evaluation with no abnormal findings. Bradipsychism and mild cognitive impairment (MMSE: 25) were noted. In laboratory testing, he was found positive for syphilis infection (VDRL+++, FTA+) and lumbar puncture yielded positive results for antibodies against spirochete Treponema. There was a mild CSF pleocytosis (CSF WBC count was 22/μl). After this, the patient was treated with intravenous penicillin G with a favorable outcome.

Discussion: Headache is common in neurosyphilis, especially in the presence of syphilitic meningitis. In this case, the only symptom was headache with occasionally migrainous characteristics that misled clinical thinking.

In conclusion, the possibility of neurosyphilis should be taken into account in the differential diagnosis of a resistant headache.

PO226

Other secondary headache disorders

Headache attributed to cerebral venous thrombosis: a case series of 36 patients in a public hospital in bogotá, Colombia

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Background: Despite advances in the recognition of CVT in recent years, the diagnosis of CVT is typically based on clinical suspicion and imaging confirmation. Because of the diversity of clinical features, diagnosis can be difficult.

Aim: Describe the clinical profile of headache attributed to cerebral venous thrombosis

Methods: We conducted an observational, descriptive, and cross-sectional study from January 2013 to August 2014. The data for all patients with headache, attending the ED at the Kennedy Western Hospital in Bogotá-Colombia were prospectively registered. Diagnosis of headache was according to the International classification of headache disorders, 3th edition (ICHD-3 Beta). The diagnosis of cerebral venous thrombosis was performed based on the guidelines of the American Heart Association and the American Stroke Association

Results: Thirty-six (5.2%) out of 688 patients with stroke had diagnosis of CVT. Ninety-six percent presented with headache, described as pulsatile (41%) or sattabing (33.3%); diffuse (37.5%) or unilateral (20.8%), and progressive (54.2%) in days to weeks (12.5 days). A migraine-like pattern was described in 62,5%. None of them had osmophobia, and autonomic symptoms were found in 8.3%. Pain tend to intensify with valsalva maneuver (58.3 %); physical activity (58.3%) and positional changes (50%).

Conclusion: In our population, headache attributed to cerebral venous thrombosis is characterized by a migraine-like pattern, apparently, the autonomic symptoms and alarm signs are the key in the differential diagnosis with primary headaches. It is still to be determined if in other studies, this clinical profile is consistent with the definitive diagnosis of cerebral venous thrombosis.

PO227

Other secondary headache disorders

Headache with neurological symptoms in a patient underwent coronary angioplasty: cardiac cephalalgia or what?

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Background: According with the ICHD-3, cardiac cephalalgia is a headache that's occurs concomitantly with acute myocardial ischemia (MI) and relieves with appropriate medical therapy or coronary revascularization. Also, other migraine-like headaches may occur with cervical arteries stenting or angiography.

Aim: To discuss the type of headache who had a patient with past history of migraine who experienced a headache with neurological symptoms when performing a percutaneous coronary angioplasty (PCA) during an acute MI.

Method: Case report

Results: A 73-year-old right handed woman who began to have migraine with sensory and/or language aura attacks at the age of 18. The patient was under treatment with simvastatin and acenocumarol. Her migraine attacks had disappeared 10 years ago. She was admitted because of acute coronary syndrome without ST elevation. Two hour later, when performing PCA she had a severe bilateral headache with nausea, dysphasia and right-sided hyposthesia. A CT scan of the brain was normal. The patient was transferred to a Stroke Unit where 60 minutes later her neurological exploration was normal. No abnormalities were found in diffusion-weighted brain MRI.

Conclusions: Confronting with a patient whose headache arose in the setting of MI is a stressful experience that brings to mind some life-threatening diseases. According to ICHD-3 our patient doesn't fulfill criteria for diagnosis of cardiac headache. Although headache attributed to cerebral angiography and cervical angioplasty exists, it hasn't been described its appearance after PCA. One last consideration is that the administration of nitroglycerin during the procedure might have triggered a migraine attack.

PO228

Other secondary headache disorders

Atypical presentation of cardiac cephalgia - thunderclap headache

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Objective: To study headache profiles in patient with cardiac cephalgia.

Background: Migraine like headache described in acuteThunderclap headache is very rare only few cases are reported. Coronary syndrome Response of indomethacin not described in thunderclap headache in cardiac cephalgia.

Method: This 40 years old male admitted with history of headache and left axillary pain since last 4 days. On history he was found to have 2 types of headache

1. Short lasting severe needle type pricking headache with left axillary pain lasting for 4–5 seconds unbearable used repeat daily around 10 times since last 4 days.

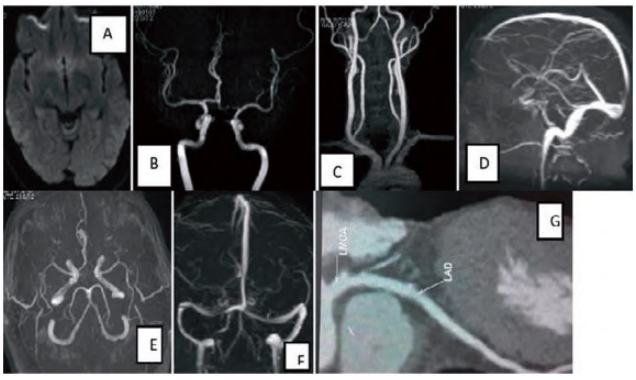
2. Second type headache is continuous holocranial headache since 1 day. No neck pain, photophobia, phonophobia. On 1 st day he had nausea and vomiting, this headache was moderate to severe,this headache used to increase with extertion like walking.

He was smoker, No history of headache or comorbidity. On examination No papilledema, No Neurodeficit.

Results: His MRI Brain, MRA, MRV was normal. ECG and cardiac troponins were normal.

He was given first indomethacin 75 mg tid after that his short lasting headache and axillary pains subsided completely,but holocranial headache was persistent After trial of nitrates headache subsided in minutes. CT cardiac angiogram shown LAD moderate stenosis.he was treated as Acute coronary Syndrome.

Conclusion: Thunderclap headache may be presentation of cardiac cephalgia which may respond to indomethacin and migraine like headache which respond to nitrates. Thunderclap headache preceds migraine like headache in cardiac cephalgia.



MRI Brain: A-DWI Brain. B,E -IC Angio, C-EC Angio. D,F MRV.Cardiac CT angiogram –G shows foca narrowing of LAD.

PO229

Other secondary headache disorders

A case of headache diagnosed with prolonged glucose tolerance test

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Introduction: Hypoglycemia symptoms start when the blood glucose in capillary blood falls (despite individual differences) to 55–60 mg/dl. If the glucose level falls below 50 mg/dl, impaired brain function occurs. The purpose of this article was to emphasize the significance of glucose tolerance test in cases of headaches that do not respond to treatment.

Case: A 30-year-old patient came to neurology polyclinic with a complaint of moderate headache which recurred every 2–3 days and which had been going on for three months on two sides of the head. Nausea-vomiting, photophobia-phonophobia and autonomic symptoms did not accompany the pain. The characteristics of the headache did not differ depending on the position. A tremor in hands accompanied the headache. The patient's history did not include diabetes mellitus. The patient did not respond to amitriptyline, venlafaxine, propranolol and valproic acid treatment. In the fourth hour of the prolonged glucose tolerance test that was administered on the patient who was checked by the internal medicine unit due to a complaint of headache, the level of blood glucose was found to be 40 mg/dl (normal value: 80–90 mg/dl).

Discussion: Hypoglycemia induced headache is a common situation. While 1988 international classification of headache included hypoglycemia induced headache, this subheading was changed into headaches associated with hunger in the classifications after the year 2004.

Conclusion: Hypoglycemia should be kept in mind in cases with treatment resistant headaches. Only after prolonged glucose tolerance test, headaches can be said to be not hypoglycemia induced.

PO230

Other secondary headache disorders

Peripheral neuromodulation for headache attributed to an upper cervical radiculopathy

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Background: Occipital nerve stimulation (ONS) is a potential approach for refractory headache attributed to an upper cervical radiculopathy (HAUCR).

Aim: The aim of this study was to assess the efficacy and safety of unilateral ONS in patients suffering from HAUCR.

Method: We conducted a retrospective chart review on patients implanted from 2008 to 2013 at the Montreal University Health Center. Data was analyzed at baseline and 12 months post implantation. The primary outcome was a 50% response rate in frequency. Secondary outcomes included quality of life (QOL), mood, patient satisfaction and disability rate assessment.

Results: Sixteen patients fulfilled the inclusion criteria, 8 men and 8 women. Mean age was 53 years old. Patients had suffered from daily moderate to severe HAUCR for an average of 18.8 years. 62.5% had developed HAUCR following a head trauma. Disability rate was high at 75%.

One year post implantation, 69% of patients were responders. 9/16 patients reverted to episodic headaches. The responder's subjective health perception on EQ-5D VAS increased by 31 points. Reduction in mean HIT-6 score was 19.6 points and only 31.25% (N = 5) of patients continued to suffer substantial to severe-impact. Patients with clinically significant depression or anxiety according to the HADS was reduced by 60%. Over 80% reported high degree of satisfaction and 37.5% (N = 6) were able to return to work. No severe adverse events were recorded.

Conclusion: Peripheral neuromodulation of the GON is a safe and effective treatment modality for patients suffering from refractory HAUCR, with significant improvement of QOL.

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Other secondary headache disorders

Ultrasound guided facet block for great auricular neuralgia: a case report

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Background: The Great Auricular Nerve (GAN) is a superficial branch of the cervical plexus arising from the anterior rami of the second and third cervical nerves. GAN neuralgia can be associated with dysautonomia such as red ear syndrome.

Aim: To describe a combined approach of GAN block and cervical facet blocks for the treatment of GAN neuralgia in a patient allergic to multiple drugs and refractory to simple nerve blockade.

Method: We performed various combinations of ultrasound guided infiltrations. For each we assessed our patient for pain on the numerical rating scale (NRS) from 0 to 10, number of paroxysmal attacks, and symptoms of dysautonomia, on a quarterly basis over a one year period.

Results: We used a 25 gauge, 3.5 inch, needle to perform an ultrasound guided GAN block that decreased her baseline pain from 5/10 to 1/10 for a six week period. An ultrasound guided C2 and C3 facet block accompanied by a suboccipital semispinalis trigger point injection induced a relief of her daily peaks of pain from 8/10 to 3/10 for a four week period as well as resolution of paroxysmal ear redness, swallowing difficulties and dyspepsia. The combination of GAN, C2 and C3 facet block provided the patient with complete symptom resolution for over 12 weeks. Oral medication were stopped. No complications were reported.

Conclusion: The combination of a C2–C3 facet block to ultrasound guided GAN block can lead to an optimal and prolonged benefit in comparison to the benefit of each technique used alone.

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Other secondary headache disorders

Differential diagnosis and treatment of myotonic and myofascial syndroms of neck pain

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Methods: The dynamic monitoring of 195 patients with myotonic and myofacial syndromes of neck pain was done against the control group of 45 people. An extended neurological examination was carried out which included roentgenometry of cervical and vertebrocranial areas of spinal column, electromyography of 7 to 9 relevant muscles, finding of the "key" muscle and the overall computer aided assessment of osteomuscular, cardiorespiratory and oxygen transport system disorders.

Results: Clinical and electromyographic criteria for diagnosis of myotonic and myofascial syndromes of neck pain were identified based on the occurrence rates. The role of major system disorders in pathogenesis of neurological manifests of neck pain was studied. New therapeutic approaches to stopping pain and myotonic syndromes were developed; the effectiveness of early rehabilitation measures was demonstrated. The prevailing myotonic syndromes were identified which were the musculus obliquus capitis inferior syndrome (in 68, or 39.4% patients); superscapular area syndrome (33% of patients); musculus scalenus anterior and musculus scalenus medius syndromes (18.9%); musculus pectoralis minor syndrome (9.7%). Hypodynamia caused system disorders were noted in 78.3% patients including excessive body mass and fat content; reduced blood circulation rate and heartbeat volume and the pronounced decrease of PWC_{170}. The most informative spondylographic findings were reduced thickness of posterior areas of intervertebral disks from CI to CVII (52.3 to 77.9% of patients), cervical lordosis impression (76.4%) and uncovertebral arthroses (58.2%).

Conclusions: The most seriously affected ("key") muscles in neck pain patients were found. Diagnosis and treatment strategies for neck pain patients were developed.

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Other secondary headache disorders

Pathogenesis of cognitive disorders in patients with initially chronic viral encephalitis

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Methods: brain MRI, research of cerebrospinal fluid and its dinamic, definition of a spectrum of 20 basic amino acids in blood serum and liquor

Results: 126 patients with initial chronic viral encephalitis were surveyed. The most significant and informative appeared the decrease in free amino acids: serine ($5{,}12 \pm 0{,}15$ mg/l; $P < 0{,}01$), glycine ($6{,}59 \pm 0{,}2$ mg/l; $P < 0{,}001$), histidine ($5{,}11 \pm 0{,}12$ mg/l; $P < 0{,}05$), alanine ($12{,}93 \pm 0{,}12$ mg/l; $P < 0{,}001$), arginine ($5{,}62 \pm 0{,}09$ mg/l; $P < 0{,}001$), tyrosine ($5{,}08 \pm 0{,}09$ mg/l; $P < 0{,}001$), meteonin ($2{,}19 \pm 0{,}12$ mg/l; $P < 0{,}001$), phenylalanine ($3{,}36 \pm 0{,}14$ mg/l; $P < 0{,}001$), lysine ($6{,}94 \pm 0{,}17$ mg/l; $P < 0{,}001$), leucine ($4{,}64 \pm 0{,}14$ mg/l; $P < 0{,}001$), threonine ($6{,}2 \pm 0{,}14$ mg/l; $P < 0{,}001$), glutamic acids ($2{,}99 \pm 0{,}16$ mg/l; $P < 0{,}001$) at simultaneous increase in concentration of tryptophan ($7{,}36 \pm 0{,}12$ mg/l; $P < 0{,}001$).

Among the connected amino acids in CMYK the reliable increase, in comparison with control group healthy participants was observed, glycine ($11{,}44 \pm 0{,}13$ mg/l; $P < 0{,}001$), histidine ($6{,}12 \pm 0{,}11$ mg/l; $P < 0{,}001$), methionine ($5{,}86 \pm 0{,}07$ mg/l; $P < 0{,}01$), lysine ($19{,}42 \pm 0{,}16$ mg/l; $P < 0{,}001$), leucine ($18{,}94 \pm 0{,}14$ g/l; $P < 0{,}01$), threonine ($18{,}94 \pm 0{,}14$ mg/l; $P < 0{,}001$), glutamic acids ($9{,}69 \pm 0{,}17$ mg/l; $P < 0{,}001$).

Conclusion: In pathogenesis of cognitive neurosis like disorders in patients with initial chronic viral encephalitis the great importance has the decrease in content of the majority free and bonded amino acids in cerebrospinal fluid and blood serum (alanine, glycine, glutamic acids, leucine, methionine, threonine, tryptophan, phenylalanine) at simultaneous increase of tryptophan, that it must be considered atcarrying out of therapeutic actions.

Keywords: Author Keywords initially chronic viral encephalitis, amino acids

PO234

Other secondary headache disorders

Treatment of medication overuse headache

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Background: MOH has an estimated prevalence of 1–2% in Europe. It has great socioeconomic costs and is considered the most invalidating chronic headache disorder whereas evidence based treatment is needed.

Aim: To review and evaluate the effect of current treatment of MOH and circumstances affecting treatment outcome.

Methods: A search on PubMed on the terms "medication overuse headache", "rebound headache", "drug induced headache" and 'headache AND drug misuse" identified 34 clinical trials relevant for this study.

Results: Advice on withdrawal of overused medication, detoxification programs and use of prophylactic medication all individually had a positive effect on treatment. MOH patients with comorbidities improved from inpatient treatment compared to outpatient treatment. Latent administration of prophylactics reduced the need of and increased sensitivity to subsequent medication. Topiramate, gabapentin and onabotulinumtoxin A as prophylactics were significantly superior to placebo in randomized clinical trials. Predictors of outcome were collected from different studies and compared.

Conclusion: Advice on withdrawal of overused medication and detoxification programs are of great importance in the treatment of MOH, but inpatient treatment should be considered for MOH patients with comorbidities. Latent administration of prophylactics reduces unnecessary use. Predictors of outcome might be used in stratification in future treatment algorithms.

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Other secondary headache disorders

Headache in cerebral venous thrombosis: a case-series

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Background: Headache happens in the majority of patients with Cerebral Venous Thrombosis (CVT, 68–90%) being sometimes the sole manifestation of the disease.

Aim: To describe the characteristics of the headache associated to CVT and to identify distinguishing features useful for an early diagnosis of this disease.

Methods: Etiological, clinical and radiological features of 25 consecutive adult patients with CVT (18 F, 7 M; mean age 40.1 yrs) were compiled from August 2005 to December 2013. Diagnosis of CVT was confirmed by brain MRI and MR-venography. All patients underwent an extensive systematic etiological and genetic work-up at admission. A structured questionnaire about the characteristics of headache was responded by all participants.

Results: Headache happened in 92% of participants, being by far the most frequent symptom (23/25, 92%). It was the sole manifestation in nearly one third of the patients (32.0%). Headache was typically severe (19/23, 82.6%) and throbbing (16/23, 69.5%), with sudden onset (13/23, 56.5%) and non-remitting (20/23, 86.9%). The sinus most frequently involved was the transverse sinus (TS) (24/25, 96.0%), either alone or in association with other sinuses.

Conclusion: Headache is the most frequent symptom and sometimes the sole presentation of CVT. Sudden onset of a severe new headache that is throbbing in quality and progressive over time, should raise the suspicion of CVT and lead to aggressive and prompt investigation.

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Other secondary headache disorders

Post-craniotomy headache after treatment of intracranial aneurysm: a cohort study comparing headaches characteristics between craniotomy and embolization

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Background: The clinical characteristics of headache attributed to craniotomy are unclear.

Aim: To determine the characteristics of headache after treatment of intracranial aneurysms.

Methods: Patients with intracranial aneurysm were interviewed before and followed for four months after treatment. We compared patients who underwent craniotomy

or embolization. All headaches occurring after treatment were included. All patients gave written informed consent, and the study was approved by the Ethics Committee in Research of the *Hospital da Restauração*.

Results: 53 patients underwent craniotomy and 48, embolization. There were no differences in headache characteristics between craniotomy and embolization group before the treatment. Headache developed within seven days more frequently after craniotomy and was also more often frontotemporal, on the same side of the surgery, with higher intensity and frequency in the first month of follow-up after craniotomy compared to embolization group. The prevalence of patients with non-migrainous headache increased in the first month after craniotomy compared to headache type previous to surgery, as well as the frequency of days with headache increased in the first month and reduced after the third month of follow-up compared to the previous pattern. The intensity of pain was higher in the first month of follow-up after craniotomy compared to the following months.

Conclusion: Post-craniotomy Headache frequently develops within seven days after surgery and is localized at the site of surgery, had non-migraine characteristics. The pain is intense and frequent in the first month, but improves by the third month of follow-up.

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Other secondary headache disorders

Secondary cases of nummular headache (NH): a case series and literature review

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Objective: To describe 2 new cases of posttraumatic NH and review the literature of NH attributable to other causes.

Background: NH is characterized by focal, fixed and well-circumscribed head pain. Though most cases arise de novo, NH onset temporally linked to secondary causes has also been reported.

Methods: Case series from Montefiore Headache Center (MHC) and literature review.

Results: Of 50 consecutive patients with NH seen at MHC, 10 had a secondary form: posttraumatic (n = 8) and postsurgical (n = 2). Of > 400 NH cases reviewed in the literature, 14 had a secondary form: intracranial lesion (n = 8), varicella zoster (n = 1), postsurgical (n = 4) and posttraumatic (n = 1). Of the 24 total secondary cases, mean age at onset was 51 (range 14–65 y/o), 67% were female, temporal pattern was continuous (n = 17) or intermittent (n = 7), shape was round (n = 14), oval (n = 9), or a bean (n = 1) ranging in size from 1.5 cm–7cm, and pain was usually unilateral (right-10; left-11), mild-moderate (75%), and located parietally (n = 13). Superimposed exacerbations of pain (46%) and sensory disturbances within the affected area (67%) occurred. Effectiveness of prophylactic treatment was variable. Treatment of the secondary cause in 3 cases led to complete pain remission.

Conclusion: NH onset may develop from a variety of secondary causes. The demographic and clinical features of secondary forms of NH seen in this case series and literature review are similar to that seen in the primary form of NH. Although the pathogenesis is uncertain, these cases support the possibility of both a central and peripheral mechanism for NH.

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Other secondary headache disorders

A case of refractory headache with antiphospholipid antibody syndrome improved by high-intensity warfarin medication

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Background: Antiphospholipid antibodysyndrome (APS) is a coagulation disorder associated with antiphospholipidantibodies. Headache is common in patients with APS and often unresponsive toanalgesics. We report a case of refractory headache in a patient with APS, whowas improved by high-intensity warfarin treatment.

Case: A 45-year-old woman visited ourhospital with severe headache over the past 1 month. Neurological examinationrevealed no abnormal findings. Brain MRI showed subacute cerebral infarction. To find an etiology of that, various antibodies associated with autoimmunedisease were checked, and antinuclear antibody, anti-cardiolipin antibody andanti-phospholipid antibody turned out to be positive. She also had a history ofspontaneous abortion on her 8th-week pregnancy. She was finally diagnosed withAPS. Hydroxychloroquine and steroid were administered. However, she complainedof persistent severe headache. Additionally, CSF analysis showed no abnormalfindings. Although NSAIDs, anxiolytics, muscle relaxant, or antiepileptic drug weretried for to attenuate symptom, there was no effect. Finally, wafarin was triedto improve her headache by achieving a prothrombin time

internationalnormalized ratio of 3.0 to 4.0 (high- intensity). Then, headache was improvedfrom severe to mild degree or nearly absent.

Conclusion: Our patient's headache was muchimproved after achieving the high-intensity INR. Headache in patients with APS. The mechanisms of the headache in patients with APS were presumed to behypercoagulability of microcirculation and thrombotic occlusion of thecapillaries, which were associated with antiphospholipid antibodies. Therefore,high-intensity warfarin could be considered as one of the treatments forrefractory headache in patients with APS.

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Other secondary headache disorders

A new drug CNV1014802 for patients with trigeminal neuralgia – a novel proof of concept, placebo controlled, randomised withdrawal study

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Background: Trigeminal neuralgia (TN) is a rare, episodic severe facial pain condition. Sodium channel blockers such as carbamazepine or oxcarbazepine are the mainstay of treatment. Although effective tolerability is poor and careful monitoring is required. CNV1014802 is a novel Nav1.7 selective, state dependent sodium channel blocker which has potential for being effective in TN.

Aim: A proof of concept study utilising a novel randomised withdrawal design to assess efficacy, and tolerability of CNV1014802.

Method: The methodology has been published (Zakrzewska et al. Trials 2013 14:402). After a run in period all patients were put on CNV1014802 and if they responded they were randomised to either active drug or placebo. Patients withdraw at any time point if efficacy is lost. Primary outcome measure pain relief and decrease in paroxysms.

Results: After screening and open label use 29 patients took part in the randomised double blind 28 day study. CNV1014802 was associated with a consistent reduction of pain and number of paroxysms in patients with trigeminal neuralgia in all primary and secondary outcomes. Treatment failure rate of 33% for CNV1014802 compared to 64% for placebo ($p = 0.097$) in double-blind. Favourable separation from placebo on the Kaplan Meier time to relapse ($p = 0.003$). No significant adverse effects and in the double blind phase the overall profile of CNV1014802 was similar to placebo with remarkably few AEs.

Conclusion: CNV1014802 now needs to be evaluated in a larger study as it has the potential to make a significant difference in pain control in TN.

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Other secondary headache disorders

Recruitment to a phase II trial for a rare disease, trigeminal neuralgia

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Background: Trigeminal neuralgia (TN) is a rare, severe episodic facial pain condition which has over the years been treated with a variety of antiepileptic (AEDs). Although effective their tolerability is poor. A new drug CNV1014802 has recently been trialled. Although the trial recruited to number it required more centres than anticipated.

Aim: Evaluate the reasons as to difficulties in recruitment and determine strategies for future trial participation.

Method: The five major initial centres kept a log all TN patients and why these patients did not enter the screening process and subsequently the flow through the trial was reviewed.

Results: From 25 centres internationally where, the 5 major centres had cohorts of 578 patients 125 patients were screened. 58 patients did not fulfil the strict inclusion criteria. Patients with severe pain preferred to go forward for surgery; others were in remission. Many patients were fearful of too many drug changes and so loosing pain control. In order to enter the trial they had to stop all AEDs except for gabapentin and pregablin which some had used unsuccessful previously. 67 patients entered the study, 44/67 (66%) completed the open label phase, and 31/44 (70%) met the randomisation criteria to enter the double blind phase.

Conclusion: For trials of rare diseases large cohorts are required which may only be found in specialist centres. Change over to new medication needs to be done quickly and the option of continuing the new drug beyond the trial would increase recruitment.

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Other secondary headache disorders

Intractable headache with autonomic features in hypophyseal macroadenoma, non-responding to treatment, a case series

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Introduction: Headaches are common sign of hypophyseal macroadenoma. Transnasal surgery and radio-surgery are common treatment modalities. In this article, severe intractable headache cases of hypophysis macroadenoma, which did not changed following surgery or radio-surgery are presented.

Case 1: A 39-year-old woman with the history of macroadenima surgery. Severe right periorbital headaches accompanied by right eye tearing, started after the surgery.

Case 2: A 36-year-old woman who had undergone surgery 4 months prior to the onset of headaches. Sever Headaches are in the left periorbital area accompanied by tearing.

Case 3: A 24-year-old female who underwent surgery six months after the onset of headaches; yet, the headaches did not change. Her headache has the same characteristics as the case 3.

Case 4: A 24-year-old female with the history of surgery 6 years ago, and radiosurgery 6 months before. The severe headaches have started recently accompanied with eye tearing.

Case 5: A 40-year-old man with history of surgery 11 years ago but it did not change the nature of his severe headaches in the right temporal area with right eye tearing.

Discussion and conclusion: Patients with hypophysis macroadenoma might develop headaches before or after trans-nasal surgery or radio surgery, which could be intractable, intense, episodic, unilateral and mostly at periorbital area with autonomic features. The question rise whether other type of surgery or other treatment modalities are needed to ameliorate headache in such cases.

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Other secondary headache disorders

Theophylline efficacy for refractory spontaneous intracranial hypotension : a case report

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Background: Spontaneous intracranial hypotension (sICH) is characterized by orthostatic headaches, low CSF pressure and/or evidence of CSF leakage on imaging. Epidural blood patches (EBP) are the usual treatment but may be unsuccessful.

Methods: We report a case of SICH with no demonstrated leak refractory to multiple undirected epidural blood patches that responded to oral theophylline.

Results: A 26 years old female presented with a 18-months progressive occipital pain radiating to the shoulders which had evolved into a chronic orthostatic headache. She complained of, dizziness, tinnitus, and hypoacousia, but no diplopia. Neurological examination was normal. Her first brain MRI with contrast showed a diffuse pachymeningeal enhancement and low lying tonsils. A diagnosis of sICH was made, and two lumbar EBPs were performed without success. Subsequent imaging including CT myelography, MRI myelography and radionuclide

cisternography failed to demonstrate a leak. Three additional undirected EBP were performed without benefit. A control MRI still demonstrated typical sICH findings. The patient was invalid and had developed cough headache attributed to the tonsillar descent. Considering its theoretical effect on intracranial pressure, oral theophylline was started. All symptoms markedly improved and the patient went back to work. This benefit was sustained 18 months later at a dose of 200 mg twice daily.

Conclusion: Theophylline may be a non-invasive and well tolerated therapeutic option for the treatment of refractory sICH when no leak is found to be addressed specifically.

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Other secondary headache disorders

Botulinum toxin treatment of headache associated with temporalis muscle hypertrophy

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Background: Temporalis muscle hypertrophy is usually related with masticatory muscle hyperactivity, attributed to temporomandibular dysfunction, chronic bruxism or parafunctional mandibular habits. Patients with temporalis muscle hypertrophy sometimes complain of headache.

Aim: To report the useful therapeutic approach with Onabotulinum toxin A (OBTx A) in two cases of temporalis muscle hypertrophy associated headache.

Method: Case 1: A 49 years old woman presented with left temporal headache started 4 years ago. Headache was recurrent, not continuous, and worsened over weeks or months with concurrent left temporal swelling. There was a swollen temporal mass on left temporal region and palpation showed painful tender points. MRI confirmed muscle hypertrophy without underlying lesions. Treatment with bite splint therapy, NSAIDs, amitriptyline and SSRI was not effective. During follow up she developed slight right temporalis hypertrophy. Case 2. A 67 years old male presented with a 6-month continuous left temporal headache. On examination there was a left temporal mild swelling with palpation tenderness. Cranial CT showed temporalis hypertrophy. There was a history of bruxism and anxiety. NSAIDs treatment obtained partial response.

Results: Case 1: Treated for over 4 years with periodic injections of 30U of OBTx A (6 points x 5U) on left temporalis and 20 U (4 points) on right temporalis with excellent response of pain for 3–6 months. Case 2 was treated once with the same pattern and pain resolved.

Conclusion: OBTx A infiltration of the temporalis muscles is an effective therapeutic alternative in the treatment of headache associated with temporalis muscles hypertrophy.

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Other secondary headache disorders

Gluten migraine

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Introduction: Celiac disease (CD) is an autoimmune enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. Both CD and migraine are the common disorders of the population. The aim of the study was to access the prevalence of migraine among CD patients.

Methods: We examined 200 CD patients and 100 patients with reflux esophagitis and without CD from the control group for the migraine. All patients fulfilled the headache diary during three months before diagnose of migraine was made and six months of the gluten diet.

Results: CD group had the migraine syndrome four times more often then the control group. In CD group the migraine attacks were 2.5 times more frequent than in control group, but the duration of the attacks was less long, 8 hours in average. The migraine attacks in CD group were less intensive by visual analog scale, 55% in average, and had a later debut. The attacks were more frequent in CD patients who were older then 50 years old. The attacks disappeared in 25% of the CD patients with migraine syndrome who were on the gluten diet and 38% had reduction of the intensity and/or the attacks frequency.

Conclusion: We revealed the clear association between the migraine syndrome and CD and the high efficiency of the agluten diet in the migraine symptoms treatment.

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Other secondary headache disorders

Headache as an initial clinical symptom of carotid artery dissection

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Background: Clinical presentation of CAD includes one side headache, pain on neck, often accompanied by Horner syndrome, and followed by cerebral ischaemia.

The aim of this study was to analyze the spectrum of clinical presentation in patients with CAD.

Methods: This was a case series of 31 patients with CAD which were hospitalized from 2001 to 2014 at our department. The CAD was diagnosed in all cases by MRI, MRA and duplex sonography.

Results: Average age of patients was 47,4 (28–59) years. From a total of 31 patients, there were 27 with unilateral and 4 with bilateral CAD. Facial and neck pain and Horner's syndrome were the only presenting symptoms in 6 patients; headache and visual disturbances in 2; headache and tinnitus in 1; facial pain, Horner's syndrome and contralateral sensorimotor deficit in 7; headache and contralateral sensorimotor deficit in 5; contralateral sensorimotor deficit in 10. CAD was spontaneous in 24 patients while in 7 was triggered by mild trauma. MRI revealed infarction in 22 patients. Between patients without brain infarction, 6 patients presenting with facial and neck pain and Horner's syndrome, 2 with headache and visual disturbances and 1 with headache and tinnitus. Good outcome (defined as modified Rankin score of 0–2) was seen in 28 patients (90,3%).

Conclusion: CAD was associated with headache in 21 patients (67,7 %). However, the clinical presentation of CAD is variable and can be similar to other etiology of stroke.

Keywords: carotid artery dissection, headache, stroke

PO246

Other secondary headache disorders

Disability is mostly predicted by headaches frequency in patients with idiopathic intracranial hypertension

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Background: IdiopathicIntracranial Hypertension (IIH) is a rare condition determined by increasedcerebrospinal fluid (CSF) pressure, and is associated with headaches, visualsymptoms and obesity. Its impact over disability is unknown.

Aim: To address the degree to which headaches frequencyand intensity, CSF pressure, depression and anxiety symptoms, and BMI predict patient-reporteddisability.

Method: Patients with IIH were assessed for CSF pressure(positive if $>$200 mmH2O), BMI (obesityif $>$30), headaches features (using the MIDAS), symptoms of depression (using the BDI-2) and ofanxiety (using the STAI-trait scale). Disability was assessed with theWHODAS-12. The ability of independent variables to predict disability wasevaluated with linear regression analysis.

Results: Twenty-two patients (20 females) were enrolled. Average CSF pressure was 297.7 mmH2O (SD 61.7; range 200–420). Average BMI was32.2 (SD 5.7, range 22.2–42). Average headache frequency/three-months was 47.6(SD 34.1; range 3–90), average pain intensity was 6.7/10. Seven patients wereclassified as depressed or dysphoric, nine anxious, thirteen obese. AverageWHODAS-12 was 27.6 (SD 11.3). Regression model explained a small portion ofdisability variation ($R^2 = .403$): headaches frequency was the mostrelevant predictor of disability variation ($\beta = .714$).

Conclusion: Patients with IIH reported considerable disability levels, that arelargely due to headaches frequency rather than CSF pressure, pain severity,depression, anxiety and BMI levels. Considering the homogeneity of scores forthe independent variables and the small sample size,

our results are open tothe discussion on the role of these variables, and need to be assessed inlarger samples.

PO247

Other secondary headache disorders

Neuroimaging findings in 60 idiopathic intracranial hypertension (IIH) patients: an Italian survey

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Background: The role of neuroimaging in idiopathic inintracranial hypertension (IIH) has not been established. Some neuroimaging abnormalities have been frequently reported in IIHpatients, and have been included among the most recently proposed diagnosticcriteria, only for patients withoutpapilledema (Friedman 2013).

Objective: the aim the study was to evaluate the presenceand the frequency of MRI and MRV abnormalities in an Italian IIH clinicalsample.

Methods: brain MRI and MRV examinations of 60consecutive patients discharged from January2012 to December 2013. with a diagnosis of IIH (confirmed by intracranialopening pressure measured in the recumbent position $\geq$200 mmH2O) were reviewed by two expert neuroradiologists.

Results: emptysella was found in 45/60 (75%); periopticsubarachnoid space distension in 46/60 (77%); optic nerve tortuosity in 24/60(40%); flattening of the posterior aspect of the globe 34/60 (57%); protrusionof the optic nerve papillae into the vitreous cavity in 16/60 (27%); narrowing of the middle of the transverse sinuses in 37/60 (62%),unilateral in 11 cases and bilateral in 26. The combination of MRI and MRV abnormalities was present in 37/60 (62%).

Discussion: our results are in line with recent literaturereports. They indicate that thediagnostic role of neuroimaging findings in IIH should be re-evaluated. Furtherstudies investigating differences inneuroimaging findings according to different subgroups of IIH patients (e.g. presence/absence ofpapilledema, presence/absence of headache, different intracranial openingpressure values) are warranted.

PO248

Other secondary headache disorders

Headache in idiopathic intracranial hypertension: are there characteristic features?

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Objective: Toinvestigate the main headache features in idiopathic intracranial hypertension(IIH).

Patients and Methods: The charts of a consecutive series of patients withIIH admitted to our Headache Center from January 2012 to May 2014 werereviewed. Diagnosis of IIH was confirmed by: absence of intracranial causativedisorders by MRI and MRV, increased CSFpressure (>200 mm H2O at lumbar puncture in the lateral decubitus position). The presence of headache and its main features were assessed by structuredinterview.

Results: Fifty-sixpatients (11 M, 45 F) with IIH and with headache were found. The most relevantheadache features were: daily or nearly-daily pain in 95%;diffuse/non-pulsating pain in 75 %; aggravation by coughing/straining in 64,2 %;at least one among nausea, photo or phonophobia in 45 %.

Discussion: Headache is the most common symptom of IIH. Recentlyproposed diagnostic criteria (ICHD-III beta version, and Friedman et al "revised criteria for pseudotumor cerebri syndrome") do not specify anyparticular headache presentation. Daily headache, diffuse, non-pulsating pain,and aggravation by coughing/straining were very common symptoms in our sample,each of these being present in more than 50% of patients; some migrainous associatedsymptoms were present to a lesser degree.

Conclusions: These findings indicate that headache attributed to IIH may in fact showsome characteristic – or at least very common – features. Further studies areneeded in order to clarify headache presentation in IIH,

also in view ofpossible proposals to integrate the current classification criteria of headacheattributed to IIH.

PO249

Other secondary headache disorders

CDH in an adult patient with craniosynostosis

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Craniosynostosis is a result of premature closure of calvarial sutures. It does exist a primary form and a second one associated with many metabolic and hematological disorders, bone dysplasia and dysostoses and ventriculovenous shunts. The prevalence rate of craniosynostosis is 3–5/10,000 live-born infants. An abnormal head shape resulting from cranial malformations in infants is a diagnostic and therapeutic challenge.

Our patient, a 27 years old female, is presented in our clinic complaining of CDH. She had a complicated at home delivery. Both parents are normal persons. No family history of craniosynostosis is evident. She began to speak at 11 years old; there is still a marked dysarthria. She never went to school. No surgical intervention is done. The imaging of the head revealed a calvaria deformity, all the sutures were closed and showed bone bridging and heaping. She has exopthtalmus, impaired vision (OD 6/10, OS 0, 06/10), dysarthria, short stature and dysmenorhea. No pyramidal, cerebelar or extra pyramidal signs are evident. The treatment with depakine was very efficient in managing the headache.

A review of literature on adult craniosynostosis and headache is done.

PO250

Other secondary headache disorders

A case of headache due to pneumocephalus after epidural blood patch

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Objective: To present a case of pneumocephalus that presented after an epidural blood patch.

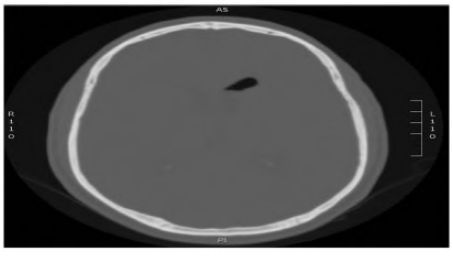
Background: An epidural blood patch is an effective method for resolving low CSF pressure headaches. In the event that a blood patch does not resolve CSF pressure headaches, physicians should take note of other rare complications such as pneumocephalus. We present a unique case of pneumocephalus after blood patch procedure.

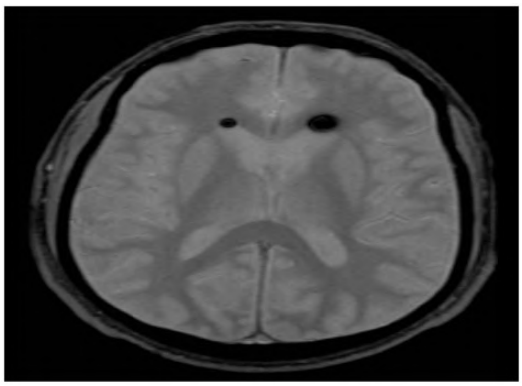
Methods: Case report

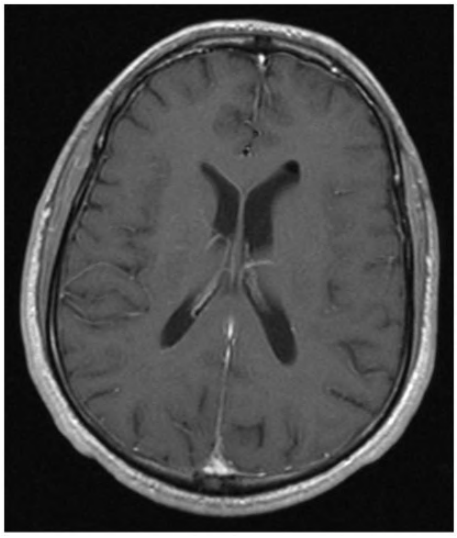
Results: 35 year old male who initially presented with headaches. Patient had an epidural injection for his chronic back pain, and subsequently developed orthostatic headache. Epidural blood patch performed. Following the procedure, headaches severely worsened. CT of the head noted 'small to moderate'' amount of intraventricular air. However the MRI was not impressive when compared to the CT, as air is difficult to visualize on MRI images.

Conclusions: MRI Scan was obtained confirming the degree of pneumocephalus but imaging characteristics were not as clear, and could have been easily overlooked without the use of CT. The MRI indicated evidence of chemical shift artifact and both DWI/GRE sequences which can be misdiagnosed by unexperienced readers as calcifications or hemorrhagic changes and could be missed on other sequences.

Pneumocephalus is a possible complication of epidural and blood patch procedures, resulting in severe headaches. Literature search suggests that this complication is either rare or goes undocumented. This case study addresses the need for physicians to be aware of rare complications during patient management. This is one of the conditions that CT has more value than MRI.







PO251

Other secondary headache disorders

Clinically-oriented stratified approach versus patient-preference stratified approach in the management of MOH – a one-year randomized trial

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Background and Aim: The management of medication overuse headache (MOH) is often difficult and no specific guidelines are available as regards the most practical and effective approaches. The aim of this study is to compare the cost-effectiveness of two different stratified approaches of drug withdrawal in 100 MOH subjects.

Methods: In the first approach, called clinically-oriented stratified strategy (COSS), patients were stratified based on the presence /absence of complicated MOH. Patients with complicated MOH received a standard inpatient withdrawal programme whereas patients with simple MOH received an advice to withdraw the offending drug. In the second approach, called patient-preference stratified strategy (PPSS), the patients received information about the effectiveness of the different withdrawal regimens: a) advice, b) outpatient detoxification and c) inpatient detoxification, and they were treated according to their preferences.

The primary outcome measures used for comparing COSS and PPSS were: 1) number of responders ; 2) number of dropouts 3) cost per detoxified patient, 4) number of relapsers at 12 months follow-up.

Results: The number of responders (80% vs 70%), dropouts (16% vs 18%) and relapsers (12.5 vs 16.6%) did not differ between COSS and PPSS. The cost per detoxified patient was 1211 € for COSS and 430 € for PPSS.

Conclusion: A patient preference stratified strategy is as effective as a clinically-oriented stratified strategy, but less cost intense.

PO252

Other secondary headache disorders

Transcranial direct current stimulation (tDCS) for the treatment of patients with secondary headache caused by recurrent unipolar nonpsychotic severe depressive disorder

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Introduction: A general rule allowing the attributionof headache to depressive disorder is the temporal connection and resolving orimproving when depression remits.

Objective: The aim of this prospective,randomized, single-blind, placebo controlled study was to resolve or improvesecondary headache, when treating recurrente unipolar nonpsychotic severedepression.

Patients and Methods: Thirty-one outpatients – 19women and 12 men, ages 21 to 40 drug-free for one month without any kind ofdrugs, with secondary headache caused by recurrent unipolar nonpsychotic severedepressive disorder. The patients randomly assigned to receive

either active(A) tDCS – 17 patients: 10 women and 7 men – or sham(s) tDCS -14 patients: 9women and 5 men.

Eight week treatment of 2-mAanodal left/cathodal right prefrontal tDCS, for 30 minutes sessions, once daily,from Monday to Friday, until the study end point. Depressive symptoms weremeasured by HDRS-17 MADRS and CGI (CGI-S and CGI-I) neuropsychological effects(MMSE) at baseline (T0) after 2nd (T1) 4th (T2), 6th (T3) and 8th weeks (T4) oftreatment. The main outcome was that pain intensity changes measured by thevisual analog scale at baseline (T0), after 2nd (T1), 4th (T2), 6th (T3) and8th weeks (T4) of treatment.

For sham conditions, the samemethod was applied, but the device was turned off.

Results: An interin analysis showed aconsistent lack of antidepressant and analgesic effects and the study wasterminated.

Conclusions: Bifrontal stimulation (leftand right DLDFC) is not effective in relieving headache caused by recurrentunipolar nonpsychotic severe depressive disorder.

PO253

Other secondary headache disorders

Adding or subtracting orthostatism: coupling anamnesis to physical exam in headache attributed to low cerebrospinal fluid pressure diagnosis

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Background: Low cerebrospinal fluid (CSF) pressure headache is usually an orthostatic headache, occurring or worsening when assuming the erect position and improving in the recumbent position.

Aim: Presentation of two cases of low cerebrospinal fluid pressure headache that demonstrate the importance of testing orthostatism for diagnosis.

Method: 1. A 45-year-old male with headache presenting exclusively in the afternoon. The patient did not associate headache with upright position. On the fifteenth day he started with horizontal diplopia.

During physical examination, headache appeared 10–15 seconds after recumbent position, and resumed shortly after standing up. He also exhibited a right sixth cranial nerve palsy.

2. A 16-year-old female with headache after a diagnostic lumbar puncture (LP), provoked with standing or sitting. Headache lasted for 4 days after the procedure; in the fifth day it became continuous, and the patient started with diplopia.

In contrast with the first days, she stopped feeling any improvement with recumbent position or worsening by standing or sitting. She also presented a bilateral sixth cranial nerve palsy.

Results: 1. An MRI showed a diffuse pachymeningeal enhancement and a bilateral subdural hygroma. The patient was diagnosed 'headache attributed to spontaneous intracranial hypotension", with an uncommon presentation: Second-half-of-the-day headache.

2. An MRA demonstrated signs of low CSF pressure, and a cerebral venous thrombosis. The patient was diagnosed 'post-dural puncture headache" and 'cerebral venous thrombosis secondary to low CSF pressure'.

Conclusion: With these exemplar and unusual cases, the authors pretend to demonstrate the importance of including orthostatism testing in headache diagnosis.

PO254

Other secondary headache disorders

Back to headache diagnose through physical examination

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Background: Physical examination is essential for the diagnosis of neurological pathology. Skipping one step of a systematic and methodical examination can lead to a delay in diagnosing potentially severe pathologies.

Aim: Presentation of an unusual case with an interesting clinical sign as the only manifestation of an intracranial dural arteriovenous fistula (DAVF), which diagnosis was delayed for 1 year due to failure to perform a complete physical exam in the initial consultations.

Method: A 68-year-old woman presented to another medical centre complaining of continuous left sided

hemicranial headache, with occasional periocular pulsatile exacerbations.

Blood analysis, electrocardiogram (ECG), Chest X-ray, cranial computed tomography (CT), and a cerebral magnetic resonance imaging (MRI) and MR angiography (MRA) were performed, all unremarkable.

The patient was treated with different medications without any improvement, and was finally referred to our hospital centre, where an auscultation of the head revealed a holocranial and facial bruit, holosystolic, more intense in the left occipital region and periocular. The examination was otherwise normal.

Results: A complete cerebral angiography was performed (figure 1), revealing a venous dural malformation to the inferior petrosal sinus, with partial retrograde drainage. An embolization of the DAVF was performed, with the definitive close of the fistula. The headache and the cranial bruit disappeared.

Conclusion: We present an unusual case of a continuous refractory headache secondary to an DAVF, and emphasize the extreme importance of a complete physical examination as a mandatory complement to a correct diagnosis in Neurology, in a medicine era based on diagnostic tests.

PO255

Other secondary headache disorders

New daily persistent headache – clinical features, comorbidities and burden in the largest german cohort

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New Daily Persistent Headache (NDPH) is a chronic headache defined with an acute onset (unremitting within 3 days). Most commonly it is described as bilaterally located headache, with mild to moderate intensity and dull quality. The persistent pain results in a severe burden of disease and restricts daily routine. Since NDPH is a rare condition clinical characteristics and burden are only blurry known.

We aimed to describe a large cohort of patients suffering NDPH regarding those features.

Patients were recruited from a tertiary headache centre (West German Headache Centre Essen), and interviewed all patients diagnosed as NDPH using a specialised questionnaire including clinical features, past medical history, and family history. Additionally changes in quality of life and psychiatric comorbidities were investigated using Head Impact (HIT 6), Von Korff graduation instrument, Hospital Anxiety and Depression Scala (HADS), short questionnaire for acquisition of stresses and strains (KFB), Sense of well-being Scala (FW 7), Beck Depression Inventory (BDI), and the German versions of the Migraine Disability Assessment Scale (MIDAS) and Patient Health Questionnaire (PHQ-D).

We were able to recruit and describe 38 patients (19 women) suffering NDPH according to ICHD-3 beta criteria. Patent age ranged between 18 to 65 years. In our cohort headache was predominantly bilaterally located (92%), and of dull character (76%). Data suggest a strong association with depression. More data will be given at the conference.

With this work we were able to investigate the largest German cohort of NDPH regarding clinical features, comorbidities, and burden.

PO257

Other secondary headache disorders

The best treatment of chronic subdural hematoma caused by intracranial hypotension

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Background: Orthostatic headache caused bylow cerebrospinal fluid (CSF) pressure of spontaneous origin(ICHD3β7.2.3) is popular headache. Almost of the headache is treated byconservative therapy. But the judgement of surgical procedure (irrigation of hematoma (IH)a nd/or extradural blood patch (EBP)) for chronic subdural hematoma(CSDH) causedby intracranial hypotension is difficult. In our research we examined the choice of thebest surgical procedure by intracranial pressure.

Method and Materials: 450 patients with orthostaticheadache by low CSF pressure of spontaneous origin visited our universityhospital. 82 patients haveipsi-/uni-lateral CSDH caused by intracranial hypotension. At the treatment ofCSDH caused by intracranial hypotension, we performed IH and/or EBP by the intracranial pressure.

Results: Group A(58 cases): IH(−) / EBP(−), Group B(5 cases): IH(+) / EBP(−),

Group C(12 cases): IH(−) / EBP(+), Group D(7 cases): IH(+) / EBP(+)

Conclusion: Both IH at intracranialhypotension and EBP at intracranial hypertension are worsening the patients-with CSDH caused by intracranial hypotension. The proper order of IH and/or EBP is depend on the intracranialpressure. We established the best treatment of CSDH caused by intracranialhypotension.

PO258

Other secondary headache disorders

Long-term efficacy of bone decompression technique combines with myo-facia decompression technique in cervicogenic headache

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Background: Cervicogenic headache (CGH) has always been considered important because of the impact on the quality-of-life and long period of illness. Bone decompression technique by using Type T bone decompression needle and facia decompression technique by using acupotomy are newly developed technique for treatment of degenerative disease and soft tissue pain. And wildly used in China.

Aim: The purpose of this study is to evaluate the therapeutic effect of Bone decompression technique combine with myo-facia decompression technique for the treatment of Cervicogenic headache (CGH).

Method: Decompression group received Bone decompression combine with facia decompression once a week for 8 weeks. The drilling tip of Type T Bone Decompression Needle is 1 mm in diameter, and it penetrated into the skull bone in 5 mm. The width of Zhendao instrument's blade for the practice of acupotomy is 0.4 mm. The control group received acupucture therapy once a week for 8 weeks. On the follow-up period, changes in the amount of pain were assessed by the VAS. Data obtained were analyzed using SPSS software.

Results: Variance analysis revealed a difference in the mean pain and disability score of the VAS questionnaire between two groups before and 1 week($P < 0.05$), 1 month($P < 0.05$), 1 year ($P < 0.05$) after the therapy. Improvement was more satisfactory in the decompression group.

Conclusion: The use of bone decompression technique combines with myo-facia decompression technique seems to have positive long-term effects on treatment of Cervicogenic headache.

PO259

Other secondary headache disorders

Syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HANDL):review and analysis of 8 cases

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Eight patients are presented (4 men, 4 women), with a mean age of 31'6 years (21–40). Most of them (71.5%) have PMH of headache (42'9% migraine, 28'6% tension headache). The most frequent neurologic deficit associated was sensory disturbance (85'6%), and aphasia (85'7%), with an average duration of the episodes between 10 minutes to 4 hours. The study of the CSF reveals pleocytosis (60–290 cels/mm3) with mononuclear predominance in 93% of the cases, and all the cases increased proteins and negative microbiologic studies are found. The neuroimaging was normal in all the cases, except for one case that reveal focal hypoperfusion conistent with the clinical symptoms, without alteration in the DWI. SPECT reveals in one case transient focal area of decreased uptake consistent with the clinical symptoms. In 71'5% of the cases the EEG shows focal transitory slowing. All the patients received sympthomatic treatment. In two cases corticosteroids were added as empiric traeatment.

PO260

Other secondary headache disorders

Hashimoto thyroiditis and headache

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Objective: Hypothyroidism can be a risk factor for the occurrence of new daily persistent headache and may also exacerbate primary headaches in some patients. The aim of this study is to evaluate the presence and clinical characteristics of headaches in patients with hypothyroidism.

Methods: Patients with hashimoto thyroiditis referred to endocrinology outpatient clinics were included to investigate the presence and prevalence of hypothyroidism related headache and primary headache.

Results: There were 158 cases in the study (10 male, 148 female) with a mean age of 43,14 ± 11,84 years. The duration of Hashimoto's disease was 74,26 ± 71,48 months. Definite diagnosis of headache due to hypothyroidism was made in 28 cases (Group 1) while a probable diagnosis was made in 11 cases (Group 2) according to their past headache stories and past abnormal thyroid function tests. 57 patients (Group 3) reported headaches which did not show any relation with thyroid functions and they were classified as migraine, tension type and other types of headaches. 62 cases reported no headache (Group4). None of the patients of migraine and TTH reported aggravation of headache with Hashimoto's disease. Group 1 and 2 patients had diffuse, squeezing headaches with mild to intermediate severity. All the patients in group 1 and 2 reported termination of headache within 3 months after the treatment of hypothyroidism.

Conclusion: We would like to emphasize that clinicians should be aware of coexistence of headache and hypothyroidism and they should search for hypothyroidism when a patient comes with a new daily persistent headache.

PO261

Other secondary headache disorders

Headache in patients with celiac disease and its response to gluten-free diet

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Background: Celiac disease (CD) is an autoimmune illness, whose prevalence is about 1% worldwide. Its relation to neurologic disturbances is well demonstrated, while its association with headache and gluten-free diet (GFD) is controversial.

Aim: To describe the characteristics of headache among celiac patients, its relationship with CD and its response to a GFD.

Methods: An online survey analyzing the characteristics of the headache and its response to a GFD in patients with CD was published throughout Argentinean Celiac social networks. The results were analyzed using chi square test or Mann-Whitney test accordingly.

Results: 1521 patients completed the survey. 866 met the inclusion criteria (mean age 39.1 ± 11.7). Patients were diagnosed with tensional-type headache (TTH, 52%), migraine with (MA, 15.4%) and without aura (M, 32.5%). 24% of the patients referred headache as the main symptom that derived in the diagnosis of CD (neurological symptoms were regarded as primary complaint more frequently among patients with MA, as compared to those with TTH)($p < 0.001$). Higher levels of improvement in headache frequency ($p = 0.02$) and intensity ($p = 0.013$) following initiation of GFD were recorded by migraineurs as compared to TTH patients.

Compliance to GFD was higher among patients with severe manifestations (77% vs. 66%)($p = 0.05$), while compliant patients showed a 48% improvement in headache frequency ($p = 0.049$). An association between food transgressions and headache was recognized by migraineurs ($p = 0.02$).

Conclusions: The percentage of migraineurs is higher among celiac patients as compared to the general population. Our results suggest that headache among these patients could improve following a GFD.

PO262

Other secondary headache disorders

Headache, focal neurologic findings and fever: a smart syndrome case

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Headache is a common consultation cause in emergency and neurology department. Patients with brain tumors have headache with special characteristics, and could be the first symptom when complications occurs.

We present a 41 years old male with history of parietal ependymoma resected in 1993 and posterior radiotherapy. One year after surgery he presented radionecrosis in irradiated field and epilepsy, so he required

ventriculo-peritoneal derivation valve and anticonvulsant therapy. There was no history of tumor recurrence. He has a slight right residual hemiparesis.

Since year 2000 he went many times to the emergency (seven admissions in 14 years) with fever, hemicranial headache and worsening in neurological examination regard baseline (worse hemiparesis and aphasia), without objective etiology of symptoms and with total recuperation each time.

In the last admission, a brain MRI showed gyriform high signal in cortical gray matter localized in parieto-occipital, insular and posterior temporal lobes without compromise of white matter in T2 and with contrast enhancement.

Other studies were normal (EEG, CSF analysis, general biochemical, serological, autoimmune and hormonal studies), so he was diagnosed with SMART syndrome (stroke-like migraine attacks after radiation therapy). He received treatment with corticosteroids and ASA with improvement.

SMART syndrome is an odd condition with prolonged and reversible headache and neurologic signs and symptoms in the years following radiation, with transient gadolinium enhancement of the cortical gyri in the previously radiated field, and not due to another disease process.

PO263

Other secondary headache disorders

Neck-tongue syndrome and its presentations

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Background: Neck-tongue is a rare yet distinctive headache syndrome that remains largely unknown and whose characterization still needs more observations.

Aim: Documentation of symptomatology to highlight diverse presentations and review of scant literature the syndrome, its underlying causes and its therapeutic approaches.

Methods: Description of case observations with symptomatology, ancillary investigations and therapeutic outcome.

Results: Association of paroxysmal pain with lingual paresthesias/hypesthesia is common but trigger factors, type and location of pain as well as underlying etiologies, vary.

Conclusion: Neck-tongue syndrome remains rare yet unique syndrome requiring proper cervicocranial anatomic assessment and whose treatment with pharmacotherapy and/or nerve block can lead to excellent outcome.

PO264

Other secondary headache disorders

Persistent primitive trigeminal artery may cause trigeminal neuralgia even on the contralateral side: review of four new cases and 20 previous ones

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Objective: The purpose of this study is to report four new cases of trigeminal neuralgia attributed to a persistent primitive trigeminal artery and systematically review the literature on this condition.

Method: Four patients (three females) aged from 22 to 50 years were seen from 1995 to 2014 by one of the authors (MMV) at the Hospital das Clínicas, Federal University of Pernambuco. A systematic review was performed using PubMed and the following keywords: trigeminal neuralgia and persistent primitive trigeminal artery.

Results: Two of our patients presented bilateral neuralgia, but the crises occurred without synchronization, and in one case there was a 6-year interval between the ipsilateral and the contralateral side of the pain. One woman reported a contralateral appearance of the pain and in the other woman the pain was ipsilateral to the persistent artery. Another 20 cases were found in the literature. The combined analysis (the 20 previously reported cases and our four cases) reveals: a predominance of females (8 men:16 women); onset at 53 ± 14 years (22–76 years, median 52 years); the pain was located on the ipsilateral side in 15 cases, contralaterally in 4 and bilaterally in 3 (2 cases with no data regarding side); the primitive artery was found on the left side in 12 cases and on the right in 9.

Conclusion: The authors propose the concept that a persistent primitive trigeminal artery can indeed cause trigeminal neuralgia on the contralateral side, sometimes triggering the pain with a bilateral (ipsilateral and contralateral) symptomatology.

PO265

Other secondary headache disorders

Behavioral assessment after induction of neural regeneration peptide 2945 on pentylenetetrazol-induced seizures in rats

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Background: Neuron Regenerative peptides (NRPs) are small synthetic peptides that stimulate neural proliferation, migration, and differentiation with low toxicity and high target specificity in CNS during diseases or injuries.

The aim of this study was to investigate the effect of NRP2945 on seizures induced by Pentylenetetrazol (PTZ) in rat models.

Methods: The effects of different concentrations of NRP2945 were tested on seizure attacks induced by pentylenetetrazol (PTZ) injection with behavioral assessment in experimental models of rat brain.

Results: NRP2945 significantly prolonged the latency of seizure attacks and reduced the amplitude and duration of epileptiform burst discharges induced by injection of intraperitoneal PTZ.

Conclusion: NRP2945 can suppress epileptiform field potentials. The results indicate the potential for NRP2945 to use in the treatment of some neurological disorders such as epilepsy.

PO266

Other secondary headache disorders

Survey regarding awareness of the disease name for medication-overuse headaches

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Objective: TheJapanese name for Medication-overuse headache (MOH) is used on a general basisfor outpatients with headaches,and it is having a certain effect. On the other hand, the Japanese name is alsothe translation for the English term "substance abuse", and it is used in governmentagencies to signify the use of drugs that are legally problematic. With theobjective of clarifying whether or not the diagnostic name formedication-overuse headaches was understood as headaches originally arisingfrom overuse of headache medicine, we carried out a questionnaire surveytargeting patients, families, and the general public. Method: The final analysis targets were 739 people. Results: On whether they had heard of the disease name before, 213people (29%) said yes, and 516 people (70%) said no. Among those who replied"yes", the responses to the question ofwhether they knew what kind of disease it was, were 90 (42%) yes, and 118 (55%)no. All respondentswere questioned regarding what kind of disease they thought it was. A –headaches due to illicit drugs such as antihypnotic agents – 394 (53%); B –headaches due to sleep medication or analgesic medication – 260 (35%); C –headaches due to headache medication – 141 (19%); with multiple answersallowed. Conclusion: It has become clear that most people believethat the Japanese term for medication overuse headache means a headache fromillicit drugs due to antihypnotic agents, so we believe that further education is necessary.

PO267

Headache epidemiology and outcomes

Headache and immigration during the economic crisis in Greece: an observational study

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Background: *In the era of economic crisis*, Greece continues receiving large inflows of immigrant population (IP) with increasingly health demands and visits in emergency departments.

Aim: To evaluate the epidemiological profile of IP headaches and the possible influence of emigration in the current stressfull sosialeconomic context.

Methods: We conducted a retrospective (24 months) and prospective study (18 months) of the visits to the emergency department at the Eginition Hospital in Greece between 2010–2012. Data collected included demographics and diagnoses according to the criteria of the IHS (International headache Society) and treatments that

had been used. Related headaches were considered to be those that began within one year of having immigrated.

Results: The IP represents 22.6% (n = 205) of the total number of visits because of headaches (n = 5988). Immigrants came mostly from Europe (17.8%). Headaches began after immigration in 40.1% of cases without the existence of any temporal relation with immigration. The most frequent diagnoses was tension-type headache (42.2%) migraine (15.5%). On comparing treatments prior to and following immigration, we find differences in the use of common analgesics (2.1% versus 46.2%), antimigraine (9.8% versus 2.1%) and in the use of preventive treatments (2% versus 45%).

Conclusions: The IP accounts for 22,6% of all first visits due to headaches and their diagnoses are similar to Greek patients. Emigration is neither a precipitating nor an aggravating factor for headaches in our series. There is a significant difference in symptomatic and preventive treatment between the period prior to immigration and afterwards.

PO268

Headache epidemiology and outcomes

Cost-effectiveness analysis of interventions for migraine in four low- and middle-income countries

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Background: Evidence of cost and effects of interventions for reducing the global burden of migraine remains scarce.

Aim: To estimate the population-level cost-effectiveness of evidence-based migraine interventions and their contributions towards reducing current burden in low- and middle-income countries.

Methods: Using a standard WHO approach to cost-effectiveness analysis (CHOICE), we modelled 26 intervention strategies including first-line acute and prophylactic drugs, and the expected consequences of adding consumer-education and provider-training. Total population-level costs and healthy life-years [HLY] gained were combined to form cost-effectiveness ratios for China, India, Russia and Zambia.

Results: Acute treatment of attacks with simple analgesics was by far the most cost-effective intervention, led by acetylsalicylic acid (ASA) which generated one HLY for < US$ 100. Adding educational actions increased annual costs by 1–2 US cents per capita of the population. Cost-effectiveness ratios then became slightly less favourable but still < US$ 100 per HLY gained for ASA. An incremental cost of >US$ 10,000 would have to be paid per extra HLY by adding a triptan in a stepped-care treatment paradigm. For prophylaxis, amitriptyline was more cost-effective than propranolol or topiramate.

Conclusion: Self-management with simple analgesics was by far the most cost-effective migraine intervention in low- and middle-income countries. Consumer-education and provider-training are expected to accelerate progress towards desired levels of coverage and adherence, cost relatively little to implement, and are also economically attractive. Evidence-based interventions for migraine should have as much claim on scarce health resources as those for other chronic, non-communicable conditions.

PO269

Headache epidemiology and outcomes

Photo-, osmo- and phonophobia in the premonitory phase of migraine: mistaking symptoms for triggers?

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Certain environmental stimuli are frequently reported as typical triggers of migraine pain. Whether these so-called triggers are independent precipitators of migraine pain or mere symptoms of the premonitory phase of migraine remains to be elucidated.

In this retrospective cohort study of 1010 migraine patients of a tertiary headache center we assessed the frequency of common trigger factors, premonitory symptoms and accompanying symptoms as well as basic headache characteristics and demographic data. Data collection and use for scientific research and publication was approved by the local ethics committee, chamber of physicians, Hamburg, Germany. All participants gave written informed consent.

Premonitory symptoms with an onset of 2 or more hours prior to the headache were present in 38.9% of migraine

patients, the most frequent being a tense neck, phonophobia and difficulty concentrating. There was a clear overlap of certain trigger factors and the presence of corresponding premonitory symptoms: flickering or bright light as a trigger was associated with higher frequency of photophobia in the premonitory phase. The same applied to the presence of food craving and osmophobia in the premonitory phase and certain foods or odours as trigger factors.

Our data thus support the view that commonly reported trigger factors of migraine are not so much independent precipitators of migraine pain, but that they are most likely just misinterpreted results of enhanced attention to certain stimuli mediated by typical premonitory symptoms of migraine pain.

PO271

Headache epidemiology and outcomes

Axis I DSM-IV psychiatric disorders in patients with migraine attending a rural based headache clinic in western India

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Background: Psychiatric disorders are common in patients with migraine. Evaluation of psychiatric comorbidity in patients with headache is often missed in the busy neurology clinics.

Aim: To assess the prevalence of Axis-I DSM-IV psychiatric disorders in patients with migraine in a rural based headache clinic in Western India.

Methods: A retrospective review of patient records of headache clinic of Shree Krishna Hospital, a rural based medical teaching hospital in Western India was done to look for associated psychiatric comorbidity. Waiver of informed consent was taken from Institutional review board for this retrospective review of records.

Results: Of 457 patients seen between July 2013 to June 2014, 237 patients had migraine. Amongst 237 patients [143 females], 123 patients had migraine, 37 patients had migraine with aura, 28 had chronic migraine, 18 had migraine with aura and 31 patients had chronic migraine with medication overuse headache. Mean duration of headache was for 3 years [range 4 months to 12 years]. 110 (46.4%) patients had depressive disorders (dysthymia or depression or suicidality), 67 patients (28.30%) had associated anxiety related disorders (generalized anxiety disorder or agoraphobia or social phobia or panic disorder), 34 (14.3%) had post traumatic stress disorder and 17 patients (7.1%) had associated psychosis. 20 of 28 (71.2%) patients with chronic migraine and 28 of 31(90.3%) of patients with medication overuse headache had an associated psychiatric disorder.

Conclusions: Axis-I psychiatric disorders are a significant comorbidity among patients with migraine and should be routinely evaluated for in all patients with migraine.

PO272

Headache epidemiology and outcomes

Prevalence of different headache disorders in a rural headache clinic in western India

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Background: No data of prevalence of different types of headache disorders in rural setting is available from India.

Aim: To assess prevalence of different headache disorders in patients attending the Headache clinic of Shree Krishna Hospital, a rural based medical teaching hospital.

Methods: Retrospective review of outpatient records of headache clinic between March 2011 to November 2014 done after taking waiver of consent from Institutional review board.

Results: Of 3293 patients seen, 3062 patients had primary headache and 123 had secondary headache. 118 patients were excluded for inaccuracy of record/incomplete evaluation. Amongst primary headaches ; 1347 had migraine [779 common migraine, 331 migraine with visual aura, 93 vestibular migraine, 13 hemiplegic migraine, 131 chronic migraine]; 1278 had tension type headache[TTH], 214 had chronic daily headache [both migraine and TTH], 63 had medication overuse headache. 78 patients had trigeminal neuralgia and 32 had trigeminal autonomic cephalalgia. 50 patients with other primary headache[6 primary stabbing headache, 3 nummular headache, 2 red ear syndrome, 13 post cough headache, 8 postcoital headache, 5 hypnic headache, 13 headache not otherwise specified. Of 123 with secondary headache; 32 had chronic meningitis, 12 had idiopathic intracranial hypertension, 19 had dural venous sinus thrombosis, 9 had sinusitis, 27 had intracranial space occupying lesion, 11 had subdural hematoma, 9 had temporal arteritis, 4 had low CSF pressure associated headache.

Conclusion: Migraine and TTH are the commonest causes of headache. Temporal arteritis is uncommon while dural sinus thrombosis and chronic meningitis are important secondary causes of headache in rural India.

PO273

Headache epidemiology and outcomes

A longitudinal observation survey on factors that affect duration of prophylactic medications for migraine in Japan setting

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Background: There are four drugs available as a prophylactic usage regularly indicated for migraine in Japan. There are not, however, any criteria and clear definition on duration of prophylactic usage at all. Therefore, there is a state quo that physicians depend upon interview of patients.

Method: In this study, to investigate relationship between duration and effectiveness, we randomly selected an approximate thousand patients with migraine (with or without), consulting our clinic for over two years. Majorities of observation taken from medical records are: 1) duration of consultation to any medical institutions after onset of migraine, 2) migraine-caused dizziness and cephalic ringing, 3) comorbidities to deteriorate migraine (potential VZV reactivation) to deteriorate migraine, 4) prophylactic medication and acute therapy. Duration toward drug deprivation was evaluated as defined by localized hypersensitivity of both occipital lobe, measured by electroencephalogram, and sufficient improvement by single use of triptan agents.

Results: Some patients experienced dizziness (approx.15%) and cephalic ringing (approx. 20%). Factors that affect duration of use of prophylactic medication for migraine are likely to be 1) aura, 2) frequency of attacks, 3) reactivating of VZV antibody. Patients who had a visit to treat within 10 years or less need to be prescribed prophylactic medicines for 6 months or a little more.

Conclusion: The longer visit to treat gets due to aging and menopausal disorders they are most likely to periods of prescription of medications shorten as attacks were reduced and tending to be transforming headache to dizziness and cephalic ringing.

PO274

Headache epidemiology and outcomes

Vestibular migraine

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Introduction: Vertigo is seen commonly in migraine patient with or without headache. This study is done to study vertigo resulting from migraine as well as other causes.

Methods: Retrospective analysis done for the headache and vertigo patients in General Neurology OPD during 1 year (1stJan 14 to 31st Dec 14), based on clinical structured interview and clinical Neuro-Otological examination.

Vestibular Migraine- (Inclusion criterias)

1. >5 episodes
2. Current or past h/o Migraine with or without aura
3. Vestibular symptoms, moderate to sever for 5 min-72 hrs
4. >50% vertigo attacks are associated with at least 1 migrainous feature
5. Not caused by any other disease.

Vertigo symptom is characterised by-

- Rotatory illusion of self
- Rotatory illusion of environment
- Head motion intolerance

Pathophysiology – is incompletely understood but plausibly could include neuroanatomical pathways to and from central vestibular structures and neurochemical modulation via the locus coeruleus and raphe nuclei.

Results-

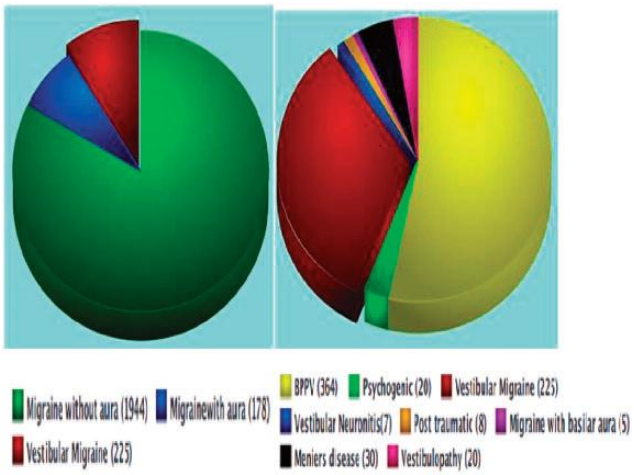
Conclusion-

- Vertigo as a migraine symptom in very common.
- Amongst Vertigo, Migrainous etiology is very common.

Observation: Attacks of Vestibular Migraine can be prevented by migraine prophylaxis, but once vertigo episode starts, sleep is most effective treatment than any acute migraine therapy or vestibular suppressants.

Suggestion- To shift 'vestibular Migraine" from Appendix to main frame of

ICHD III beta, as vertigo is very common symptom



PO275

Headache epidemiology and outcomes

Prevalence of migraine amongst patients with acute ischemic stroke in a rural based medical teaching hospital in western India

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Background: Migraine may be a risk factor for ischemic stroke but its exact role is debatable.

Aim: We aimed to assess frequency of migraine amongst patients with ischemic stroke in a rural based medical teaching hospital.

Methodology: Consecutive patients admitted between Jan 2012 to March 2013 with ischemic stroke were evaluated for presence or absence of migraine on the basis of ICHD 2 classification. Data regarding other risk factors were also evaluated.

Results: Amongst 287 patients admitted with ischemic stroke [124 males], [mean age 64(23–93)], 29 (10.1%) patients had migraine. 13[44.8%] of these 29 patients had migraine with aura. There was no difference between conventional risk factors profile of patients with and without migraine. Migraine was not a significant risk factor for stroke in the overall group. However amongst young stroke patients [Age].

Conclusions: The frequency of migraine amongst all patients with ischemic stroke is less compared to its community prevalence. However, amongst young onset stroke, migraine with aura may have an important role in combination of other risk factors.

PO276

Headache epidemiology and outcomes

Spectrum of headache disorders amongst patients with rheumatologic disorders in a rural based medical teaching hospital in western India

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Background: The relationship between headache and rheumatologic disorders is not clearly defined.

Aim: We aimed to assess spectrum of different headache types in patients with Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjogren syndrome, mixed connective tissue disease (MCTD) and Antiphospholipid syndrome (APLA).

Methods: 39 patients with rheumatologic disorders [13 SLE, 14 RA, 4 MCTD, 4 Sjogren syndrome, 4 APLA] were evaluated for headache between Jan 2013 to October 2014 in medicine and neurology departments of Shree Krishna Hospital, a rural based medical teaching hospital in Western India. Individual disorders were diagnosed on the basis of American College of Rheumatology [ACR]. Headache classification amongst these was done using the ICHD-3 beta classification. Only patients with >4 scores on visual analogue scale (VAS) were classified for different headache types and included in this study.

Results: 31 patients had a primary headache disorder. Of these, 12 [38.7%] had migraine, 13 [41.9 %] had tension type headache, 4 had cervicogenic headache, 1 patient had trigeminal neuralgia, 1 had persistent idiopathic facial pain. 8 patients had secondary headaches which were related to infarct [2], cerebral venous sinus thrombosis [2], 2 had focal pachymeningitis with superior orbital fissure syndrome, and 2 had lupus cerebritis. All patients with associated red flags [either of confusion, seizure, focal deficit, optic disc edema] had secondary headache.

Conclusion: Primary headache is frequent in patients with rheumatologic disorders. Secondary headache disorders should be ruled out in all patients with rheumatologic disorders with associated red flags.

PO277

Headache epidemiology and outcomes

Prevalence of headache in nepal: a nationwide population-based study

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Background: Headache disorders are of global public-health importance. At country level, health policy depends on knowledge of the health of local populations. The South-East Asia Region (SEAR) is one of two of WHO's six world regions for which no national headache prevalence data are available. Our aim was to estimate 1-year and 1-day prevalence of headache in Nepal, a country within SEAR.

Methods: In a cross-sectional survey, we randomly sampled 2,100 adults, representative of the Nepali-speaking population aged 18–65 and living in Nepal. Structured face-to-face interviews used a culturally-adapted version of the Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire. Informed consent was obtained in accordance with the requirements of the review boards for research ethics in Nepal and Norway.

Results: The 1-year prevalence of any headache was $85.4 \pm 1.5\%$, with significant associations with female gender (OR 1.9; 95% CI 1.54–2.53) and age ($p = 0.023$), peaking in the range 46–55 years. Headache was more common in urban areas (OR 1.6; 95% CI 1.18–2.17). The prevalences of headache on $\geq$15 days/month and probable medication-overuse headache were $7.7 \pm 1.1\%$ and $2.2 \pm 0.63\%$ respectively. The 1-day prevalence (headache yesterday) was $17.9 \pm 1.6\%$, higher among women than men ($21.5 \pm 2.8\%$ *versus* $13.4 \pm 2.3\%$; OR 1.8; 95% CI 1.42–2.30) and significantly associated with age ($p = 0.014$), peaking between 46–55 years.

Conclusion: Headache disorders, including those occurring on $\geq$15 days/month, are very common in Nepal, and of major public-health importance as elsewhere in the world. This new evidence will inform national health policy and provide a basis for health-care needs assessments.

PO278

Headache epidemiology and outcomes

The study of the prevalence of headache among medical students

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Background: The problem of headache among students has medical and social character because it affects the performance and efficiency of the student during the training period, and therefore they are subject to a maximum psycho-emotional and intellectual stress, especially during the delivery of tests and examinations. In turn prolonged exposure to these stressors leads to an increase in the frequency of complaints of headache among the students.

Aim: To study the prevalence of headaches in medical students.

Material and methods: The object of the study was 510 students of the Kyrgyz State Medical Academy 19–24 years studied in the 4th year of medical faculty. The study was conducted at the Department of Neurology with a course of medical genetics under KSMA between September and December 2014. Students were interviewed by a special modified questionnaire on headache.

Results: Analysis of the questionnaires revealed that complaints of headaches presented 204 people- 40.0%. Among them, the girls complained of headaches 73.0%, young men – 27.0%. During the analysis of the data revealed that the frequency of occurrence of primary headache – a tension type headache (50.9%) has the first place, followed by – cervicogenic headache (16.9%), followed by unspecified cephalic syndrome (16.5%) and migraine (15, 7%). Found that gender was significantly direct impact on the incidence of headache – the girls headache is more common (73.0%) than boys (27,0%) ($p < 0{,}005$).

Conclusion: Among the primary headaches students prevails tension type headache −50.9% and females headache is more common than in men by more than 2 times.

PO279

Headache epidemiology and outcomes

Off-label and non-recommended migraine medication in the outpatient clinic

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Background: Off-label medications are widely used in headache patients and frequently endorsed by scientific societies. Even prescribed in the patient's best interest, its use may raise legal and reimbursement issues. Furthermore, the legally approved indications vary among countries. It's of paramount importance to evaluate the off-label and non-recommended prescription rate by country and its usefulness.

Aim: To present off-label and non-recommended medication frequencies in migraine treatment and assess its effectiveness.

Method: Retrospective observational study including migraineurs in a general neurology clinic during three years. We collected data on symptomatic and prophylactic medications used. We reviewed the summaries of product characteristics, European and Portuguese guidelines for approval and endorsement in migraine. Effectiveness was defined as benefit reported by the patient and 50% frequency reduction.

Results: We identified 102 migraineurs (79.4% female, mean age 40.1 years), 41.2% with aura. 194 symptomatic and 106 prophylactic medications were used.

Among symptomatic medications, 9.3% were off-label, 6.7% outside European recommendations and 11.8% without national guideline support. For prophylactic drugs these proportions were 16.0%, 1.9% and 5.7%. 4.1% of symptomatic and 1.9% of prophylactics were given without any regulatory or scientific endorsement.

There was no significant difference in effectiveness between approved/recommended and non-approved/non-recommended symptomatic drugs. Off-label prophylactic medication was less effective than approved counterparts ($p = 0.036$).

Conclusion: Our off-label prescription frequency was lower than other headache studies, however we only analyzed migraine, which has more approved medications. Non-sanctioned symptomatic drugs were equally effective, probably due to analgesic class effect. There was no gain in using non-approved prophylactics.

PO280

Headache epidemiology and outcomes

Migraine referral according to European headache federation levels of care: an exploratory analysis

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Background: The EHF recommends the organization of health services to headache patients as a three-level model involving primary and secondary care. In Portugal these recommendations are seldom followed and referral criteria aren't universal. Due to that, patients with different levels of complexity attend tertiary centres.

Aim: To stratify migraineurs referred to a Neurology outpatient clinic according to EHF recommended levels of care. To evaluate the demand for a Headache consult.

Method: Retrospective observational study including migraineurs in a general neurology clinic during three years. We established transition rules between levels of care. These could be lenient (level 3: brainstem/motor aura, failure of 2 prophylactic drugs, medication overuse headache, and/or chronic migraine; level 2: other auras, headache frequency 4–14 days/month, failure of 2 symptomatic or 1 prophylactic drugs, and/or difficult differential), or stringent (level 3: same as before excluding chronic migraine and increasing failure to 3 prophylactics; level 2: all migraine frequency >3 days/month, and failure of 3 symptomatics).

Results: We identified 102 migraineurs (79.4% female, mean age 40.1 years), 41.2% with aura.

With criteria allowing easier access to upper levels of care we identified 10.8% patients in the first level, 54.9% in the second and 34.3% in the third. Applying more restrictive criteria these percentages were 27.5%, 53.9% and 18.6%.

Conclusion: At least 10% of patients could be followed by primary care physicians, and up to 30% with proper advice and education. Outside primary care the existence of 1/5 to 1/3 of patients who fit level 3 criteria demands a specialized consult.

PO281

Headache epidemiology and outcomes

Situation of the headache service in a developing country: Egypt

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Introduction: Headache on its own ranks among the top causes of years of life lived with disability (YLD). The epidemiology and experiences of patients with headache disorders in the developing world are uncertain, because the majority of research on headache disorders comes from a limited number of high-income countries. Most middle and low income countries published nothing about headache.

Methodology: This work represents an observational study upon the headache service provided at Cairo/East-Egypt among 3 sectors (1st is public university hospital specialized Headache Clinic, 2nd is Private Hospitals and 3rd is Private Specialized Headache Centers and Private Clinics).

Objective: To have a preliminary idea about the situation of headache disease burden, services and awareness among these areas. To identify some of the barriers among middle and low income countries.

Outcomes: (1) The average number of patients seeking medical advice for headache at this area and their demographical analysis, (2) The average cost of the headache service in developing countries. (3) Services offered to patients with headache(pharmacological and non pharmacological) in Egypt (4) Patient and physicians awareness about headache and their perception for the new therapeutic tools (5) Barriers against headache service in Egypt.

Conclusion: Some countries may have higher than expected numbers of headache sufferers than experts could predict. Treatment strategies and programs based on data from wealthier settings may not be generally applicable when they are introduced globally.

PO282

Headache epidemiology and outcomes

Short sleep duration is associated with an increased headache frequency in migraineurs: a population-based study

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Background: Sleep deprivation has been reported to affect various physiological functions including brain. Short sleep duration on regular base is considered to be a chronic sleep deprivation state. However, the association between short sleep duration and headache/migraine has rarely been reported.

Aim: This study is conducted to investigate the association between short sleep duration and clinical characteristics of migraine using the Korea Headache-Sleep Study data.

Methods: We selected a stratified random population sample of Koreans aged 19–69 and evaluated them with a semi-structured interview designed to identify headache type, clinical characteristics of migraine and sleep duration. We defined short sleeper as participants sleeping $\leq$5 hours on weekdays.

Results: Of 2,762 participants, 147 (5.4%) were diagnosed as having migraine during the previous year and 219 (7.9%) participants were classified as short sleepers. Migraine prevalence was not significantly different between short sleepers and non-short sleepers (6.4% vs. 5.2%, $p = 0.462$). Mean sleep duration (7.1 ± 1.4 vs. 7.1 ± 1.3, $p = 0.669$) and proportion of short sleeper (9.5% vs. 7.8%, $p = 0.462$) were not significantly different between migraineurs and non-migraineurs. Migraineurs with short sleep duration reported higher headache frequency per month (8.4 ± 10.2 vs. 3.6 ± 6.0, $p = 0.024$) compared to migraineurs without short sleep duration. Visual analogue scale for headache intensity (6.5 ± 1.8 vs. 6.2 ± 2.0, $p = 0.543$) and Headache Impact Test-6 score (58.1 ± 10.0 vs. 54.0 ± 9.2, $p = 0.061$) were not significantly different according to short sleep duration among migraineurs.

Conclusions: Five or less hours of sleep duration is associated with an increased headache frequency. Our study suggest that short sleep duration may exacerbate migraine.

PO283

Headache epidemiology and outcomes

Migraine and restless legs syndrome are associated in early adulthood and midlife but not in elderly group: a population-based study

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Background: Recent studies have shown a close association between migraine and restless legs syndrome (RLS). Unlike migraine, RLS prevalence increase with the increase of age and peaks after 50 s. However, the comorbidity of migraine and RLS according to age group has rarely been reported.

Aim: This study is to investigate the comorbidity between migraine and RLS according to age group using the data of Korea Headache-Sleep study, a nation-wide population-based cross-sectional study.

Methods: We selected a stratified random population sample of Koreans aged 19–69 and evaluated them with a 60-item semi-structured interview designed to identify headache type and RLS. We used 2003 International Restless Legs Syndrome Study Group criteria for the diagnosis RLS. We classified age groups as early adulthood group (19–34 years), midlife group (35–49 years) and elderly group (50–69 years).

Results: Of the 2,762 participants of the Korean Headache-Sleep Study, the 1-year prevalences of migraine and RLS were 5.4% and 5.5%, respectively. For all ages, RLS was positively associated with migraine [odds ratio (OR) = 1.8, 95% confidence interval (CI) = 1.2–4.2, p = 0.012] compared to non-headache control. Among early adulthood age group (OR = 7.8, 95% CI = 2.0–30.5, p = 0.003) and midlife group (OR = 6.2, 95% CI = 2.1–18.6, p = 0.001), migraine showed a positive association with RLS. Migraine and RLS did not show a significant association in elderly group (OR = 0.9, 95% CI = 0.3–3.0, p = 0.366).

Conclusions: Our result suggests that migraine and RLS are differently associated according to age group.

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Headache epidemiology and outcomes

Clinical characteristics of migraine in a Taiwan clinic

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Background: To identify the migraine characteristics in headache clinics in Taiwan

Methods: We collected 208 migraine patients from a headache special clinic during February 2012 to February 2013. Migraine was diagnosed according to the ICHD-2 criteria and classified into episodic migraine (EM), chronic migraine (CM), and medication-overuse headache (MOH). Their disability was evaluated by the Migraine Disability Assessment (MIDAS) score, and further classified into four grades.

Results: A total number of 208 patients were enrolled, including 129 EM (20.2% had aura in EM groups), 62 CM, and 17MOH. Their MIDAS distributions were 19 in Gr I, 26 in Gr II, 48 in Gr III, and 115 in Gr IV. Most patients were female (83.7%), and their mean age was 41.9. The mean duration of headache was 15.8 years. Headaches were reported unilateral in 41.3% patients, and pulsatile features in 45.2%. Overall, 79.3% patients had nausea, 47.6% had photophobia, 68.3% had phonophobia, and 80.8% patients avoided routine physical activities while migraines attack. Female patients tend to have more phonophobia (71.3% vs 52.9%, p = 0.036) and more easily to avoid physical activities (83.9% vs 64.7%, p = 0.009) than males.

Conclusions and Recommendations: Our study offers the epidemiological characteristics of migraine, which may help not only our daily clinical practice in clinics but also primary care physicians in Taiwan.

PO285

Headache epidemiology and outcomes

Probable diagnosis in patients with primary headache disorder by the 3rd beta edition of international classification of headache disorder: a multi-center study in Korea

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Background: According to the 3rd beta edition of International Classification of Headache Disorder (ICHD-3 b), probable primary headache disorder (PPHD) is diagnosed when headache fulfilling all but one criteria of primary headache disorder (PHD). Diagnosis of PPHD can happens in condition of incomplete or atypical presentation of PHD. We investigated prevalence and clinical characteristics of PPHD among first-visit patients for headache.

Methods: Eleven neurologists from university or regional hospitals enrolled consecutive first-visit patients for headache. The classification of headache disorder was done according to ICHD-3β by each investigator based on the initial evaluation or by a consensus meeting for the uncertain cases. The proportions of probable diagnosis were assessed and the clinical characteristics of patients diagnosed as PPHD were compared to patients with definite PHD.

Results: A total of 999 patients with PHD were enrolled and 202 (20.2%) had PPHD. The proportion of PPHD was the highest in tension-type headache (Migraine, 14.8%; tension-type headache, 33.8%; trigeminal autonomic cephalalgia 20%; other PHD, 12.8%). Patients with PPHD had less severe headache intensity (5.7 ± 2.1 vs 6.5 ± 2.0, $p < 0.001$), and had shorter duration of headache from the onset (median 1 vs. 3 months, $p < 0.001$) than those with definite diagnosis. Current age and route of visit were not different between two groups. Common missing criteria in PPHD were total frequency (9.4%), duration of attack (3.8%), and associated symptoms (2.3%).

Conclusions: Diagnosis of PPHD was consisted 20.2% of the PHD among first-visit headache patients. Missing total frequency criteria is the most common cause for probable diagnosis.

PO286

Headache epidemiology and outcomes

Prospective evaluation of determinants of choice of medication in migraine prophylaxis and prevalence of refractory migraine after appropriate therapy

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Aims: To prospectively evaluate the prevalence of associated co-morbidities and contra-indications to particular drugs which influence choice of migraine prophylaxis. To assess prevalence of Refractory migraine, after appropriate double-medication prophylaxis, at 6 months' follow-up.

M&M-

109 migrainous patients (mean age 32, 67% females, 27% with aura) were assessed.

Co-morbidities and preferred medications noted-

Epilepsy- (Valproate, Topiramate)

Vestibular migraine- Flunarizine

Depression- Amitryptiline

Hypertension, IHD- Betablockers

Contra-indications noted:

Diabetes, Asthma – Betablocker

Young women- Valproate

Obesity- VPA, Flunarizine

Patients with relevant co-morbidity received appropriate drug. Randomisation to medications was done after noting contra-indications. The distribution was- Amitriptyline 25/109(22.93%), Propranolol 27/109(24.77%), Valproate 22/109(20.18%), Flunarizine 32/109(29.36%) and Topiramate 3/109(2.75%). At each visit, 'improvement' denoted reduction of headache frequency and severity (visual analog scale) over 30% from last evaluation. Standard abortive medications were used.

Results: Associated disorders were seen in 18.6% patients (Vertigo 50%, Hypertension 20%, Epilepsy 15%, Depression 10%, IHD 5%, obesity 11 %).

67.4% had one or more contra-indications to medication(youngfemale 89.8%, Diabetes 8.4%, Asthma 5%, Cardiac failure 1.5%).

30.2% (33/109) patients were truly randomisable to any prophylactic medication.

Statistically, all the 5 prophylactic medications showed similar efficacy at 3 months. Sustained improvement over 3 months was seen maximally in Flunarizine group (48%, vs 31–34% for other prophylactics). Significant improvement in 1st month itself was seen maximally in Propranalol(17.8%).

17/109 patients remained unimproved at 3 months and needed 2nd drug. At the end of another 3 months, 4 (3.66% of original 109) remained unimproved, denoting Refractory migraine.

PO287

Headache epidemiology and outcomes

Onabotulinumtoxin-a injection and patient reported outcome

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Objective: Do chronic migraineurs have favorable patient reported outcomes after at least 2 sessions of onabotulinumtoxinA (onabot) injections?

Method: Chronic migraineurs receiving onabot were identified. Patient Health Questionnaire-9 (PHQ-9), European Quality of Life, 5-Dimension (EQ-5D), Headache Impact Test (HIT6), and Pain Disability Index (PDI) were reviewed across $\geq$2 consecutive onabot injections for 6–12 months. Paired t-Tests on patient's questionnaire scores before and after treatment were performed. Patients were stratified for PHQ-9, and those with baseline scores $<$10 were not considered.

Results: 429 patients met our inclusion criteria from 2010 to 2014. Average age was 45 years, with 85.5% female, and 92.1% Caucasian. There were 127 patients with PHQ-9 scores $\geq$10 at baseline. Their PHQ-9 scores improved from 14.4 [high-moderate] pre-onabot to 11.3 [low-moderate] post-onabot ($P < 0.0001$, 95% CI $= -4.2$ to -2.1); PDI improved from 4.3 to 3.8 ($P < 0.0078$, 95% CI $= -0.7$ to -0.1); EQ-5D improved from 0.74 to 0.77 ($P < 0.0078$; 95%CI $= 0.01$ to 0.04); HIT6 improved from 63.3 to 60.5 ($P < 0.0001$, 95%CI $= -3.4$ to -2.2). For comparison, in the PREEMPT onabot regulatory trials, HIT6 changed from 66 to 61.2 after 5 onabot injections at 24 weeks, $p < 0.001$.

Conclusion: Onabot injection in chronic migraine patients improved headache and quality of life, and decreased impact of headache on daily life as well as demonstrating statistically significant improvement in depression scores.

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Headache epidemiology and outcomes

One questionnaire to diagnose most of the primary headaches: the prilevel pilot study

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Background: The results of epidemiological studies in the field of primary headaches (PH) vary to some extent, not covering all world's regions. The prevalence of headache in Estonia has never been investigated. Estonia is one of the leading countries in the world regarding the availability and usage of internet and web-based solutions per household.

Aim: The aim of this study is to validate an online questionnaire which will be used in a nation-wide epidemiological study to estimate the prevalence of PH in general population in Estonia.

Methods: An online questionnaire was compiled. Its first part was designed to collect demographic data and lifestyle factors of participants. The second part – the diagnostic one – consists of 14 questions (based on the ICHD-3 beta criteria) targeting different aspects of the persons' headache. Based on these answers, a specifically designed algorithm provides the probable diagnosis, whenever possible. The algorithm strictly uses the ICHD-3 beta criteria to

recognize PHs, trigeminal neuralgia/neuropathy, headache attributed to traumatic injury to the head and medication overuse headache. The study was approved by the Research Ethics Committee of Tartu University.

Results: To calculate the validity of the questionnaire and the algorithm, consented patients, who have received a definite headache diagnosis by a headache specialist at Tartu University Hospital's Headache Clinic during 2014 will fill the questionnaire. The sensitivity, specificity, positive and negative predictive value for every PH disorder in the algorithm will be presented.

Conclusion: Web-based questionnaires can provide a reliable tool for performing epidemiological studies.

PO289

Headache epidemiology and outcomes

Use of aspirin combinations with caffeine and increasing headache frequency: a prospective population-based study

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Background: Combinations of analgesics with caffeine were discussed to bear a risk for headache chronicity.

Aim: We investigated if aspirin with caffeine (ASA+) increases headache frequency compared to aspirin alone in migraine, tension-type headache (TTH) and migraine + TTH (MigTTH).

Method: The population-based German Headache Consortium Study, participants aged 18–65 years, collected information about headache and analgesics at baseline (2003–2007, t_0, response rate: 55.5%), fist follow-up after 1.87 ± 0.39 years (t_1, 37.2%), second follow-up after 3.26 ± 0.60 years (t_2, 38.8%). We included participants with headache at t_0, aspirin intake, ASA+ or no analgesics at t_0 and t_2 and known headache frequency. Linear regression was used to estimate changes of headache frequency ($\Delta t_2 - t_0$) and 95% confidence intervals (95%CI) depending on analgesic intake, stratified by headache subtypes, adjusting for sex, age, analgesics at t_1, changes of headache frequency at t_1, drinking, smoking, BMI, education, headache frequency at t_0.

Results: Out of 509 participants (56.0% women, 42.0 ± 11.8 years), 45.2% reported aspirin intake (41.3 ± 10.9 years, 59.6% women, headache days at t_0: 2.8 ± 3.1 days/month, t_2: 3.6 ± 4.1 days/month), 11.8% ASA+ intake (46.0 ± 9.8 years, 73.3%, t_0: 4.8 ± 6.1 days/month, t_2: 5.3 ± 5.1 days/month), 43.0% no analgesics (41.6 ± 13.1 years, 47.5%, t_0: 3.8 ± 6.2 days/month, t_2: 5.3 ± 6.6 days/month). There was no increase in headache frequency in participants with ASA+ intake compared to aspirin [adjusted, all headache: 0.04 days/month (95%CI: −2.23; 2.31), migraine: −1.36 days/month (−4.76; 2.03), TTH: −0.57 days/month (−4.97; 3.84), MigTTH: 2.46 days/month (−5.19; 10.10)] or no analgesics [all headache: −1.30 days/month (−3.79; 1.19), migraine: −3.77 days/month (−9.22; 1.68), TTH: −4.86 days/month (−9.62; 0.27); MigTTH: −3.22 days/month (−10.16; 3.71)].

Conclusion: In our study ASA+ intake did not increase headache frequency compared to aspirin or no analgesics.

PO291

Headache epidemiology and outcomes

One-year prevalence of migraine using a validated extended french version of the ID migraine-TM: a Belgian population-based study

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Background: Country-specific prevalence data on migraine and comorbidities are vital to assess the public health burden of migraine and the corresponding resources management required. In absence of reliable statistics, this study aimed to estimate the one-year prevalence of migraine in Wallonia (Belgium) in relation to sociodemographic factors and several health indicators.

Methods: Among the 1071 participants aged 20–69 years of the NESCaV survey, 751 (70.1%) were screened for one-year migraine attacks by the "ef-ID Migraine", a validated, extended French version of the self-administered ID Migraine™ questionnaire. Sociodemographic and health data were collected by an auto-administered questionnaire and a clinical examination.

Results: The overall one-year prevalence of migraine was 25.8% and 40.8% of migraineurs reported visual symptoms compatible with an aura. The prevalence was higher in women of reproductive age (33.9%) than in men (17.9%) of the same age. Importantly, migraine was associated with the subjective feeling of poorer health. No other socio-demographic factor and health indicator studied were significant.

Conclusions: High prevalence of migraine and strong association with poor health feeling should incite health authorities for more active public health and management policies with regards to the migraine problem.

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Headache epidemiology and outcomes

Examination of fluctuations in the atmospheric pressure related to migraine

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Introduction: Japanhas four seasons and many chances of low atmospheric pressure or approaches oftyphoon, therefore it has been empirically known that the fluctuation of weather inducesmigraine in people. Generally, its mechanism has been interpreted as follows: physicalloading, attributed by atmospheric pressure to human bodies, compresses ordilates human blood vessels, which leads to abnormality in blood flow andinduces migraine. We report our examination of the stage in which migrainetends to be induced focusing on the variation of atmospheric pressure. [Subjects]Subjects were 34 patients with migraine, who were treated in our hospital. The patientsincluded 31 females and three males, whose mean age was 32 ± 6.7. 22 patientshad migraine with aura and 12 patients had migraine without aura. [Method] Allof subjects with migraine maintained a headache diary to record atmosphericpressures when they developed a migraine. The standard atmospheric pressure wasdefined as 1013 hPa, and with this value as the criterion, we investigated slightfluctuations in the atmospheric pressure when they developed a migraine. [Result]It was found that the atmospheric pressure when the patients developed a migrainewas within 1004–1009 hPa in the approach of low atmospheric pressure and that thepatients developed a migraine when the atmospheric pressure decreased by 4–9 hPa, slightly less than the standard atmospheric pressure. [Conclusion] It wassuggested that triptan formulations should be available to the patients whenthey are in the circumstances with slight fluctuations in the atmospheric pressure.

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Headache epidemiology and outcomes

Walk and tandem walk agility in migraine patients

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Background: Migraine is associated with ischemic complications that cause tissue damage of cerebral white matter of the cerebellum and vestibular system, especially in presence of aura. Some studies reported balance and motor cordination alterations, suggesting a clinical impairment caused by migraine.

Aim: To assess the performance of walk (WT) and tandem walk (TWT) tests in patients with migraine.

Methods: Were evaluated 35 migraine patients without aura (M), 35 with aura (MA), 35 with chronic migraine (CM) and 30 control patients (CG). The migraine patients were screened from a headache outpatient clinic and diagnosed by neurologists according to ICHD-III. Were excluded all subjects with systemic diseases, high BMI and history of vestibular diseases.

A blind evaluator assessed the WT and TWT velocities (cm/sec) on Balance Master System (Neurocom®) composed by a 1,40 meter force platform. The patients were instructed to walk three times at their fastest speed 1 meter before to 1 meter after the platform at the WT, and across a line over the platform at the TWT. The groups were compared by ANOVA for unpaired data (Tukey post-hoc) using the software GraphPad Prism 5.

Results: Patients with migraine performed the WT slower than CG ($p < 0.0001$), without differences between the migraine groups. The same occurred at the TWT ($p < 0.0001$), without differences between the migraine groups except for MA vs. CM (Table 1).

Conclusion: Migraine patients have lower velocity to walk and walk across a line suggesting a premature deterioration of the postural control system.

Table 1. Mean Difference and 95% CI of Walk and Tandem Walk Test velocity(cm/sec) in all groups

	Walk Across Test		Tandem Walk Test	
	Mean diff.	95% CI	Mean diff.	95% CI
CG vs. M	16.47	10.32 to 22.62*	8.153	6.115 to 10.19*
CG vs. MA	18.6	12.46 to 24.75*	6.488	4.450 to 8.526*
CG vs. CM	19.14	12.99 to 25.28*	9.001	6.963 to 11.04*
M vs. MA	2.134	-4.013 to 8.282	-1.666	-3.704 to 0.3723
M vs. CM	2.667	-3.481 to 8.814	0.8476	-1.190 to 2.886
MA vs. CM	0.5324	-5.615 to 6.680	2.513	0.4753 to 4.551*

CG: Control Group, M: Migraine Group, MA: Migraine with aura Group, MC: Chronic Migraine Group. *$p<0.01$.

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Headache epidemiology and outcomes

Clinical features of migraine and tension-type headache in Korea: a single center experience

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Objective: To analyze the epidemiological and clinical characteristics of migraine and tension-type headache (TTH) in secondary referral hospital of Korea.

Methods: 625 patients were recruited prospectively; episodic migraine (26.9%), probable migraine (5.1%), episodic TTH (21.3%), probable episodic TTH (6.6%), primary chronic daily headache (19.4%), and other primary headache (15.7%). We analyze the clinical characteristics of episodic migraine and episodic TTH.

Results: The mean age at onset was 24.6 ± 9.2 years in migraine and 37.9 ± 14.5 years in TTH ($p < 0.05$). Female sex was more prevalent in migraine ($p < 0.05$). Migraine headaches were unilateral (57%), pulsating (52%), aggravated by physical activity (80%), and were accompanied by vomiting (58%), photophobia (70%), and phonophobia (76%). TTH were unilateral (55%), pulsating (18%), aggravated by physical activity (23%), accompanied by photophobia (22%) and phonophobia (33%). The most frequently reported trigger factors for migraine were stress (82%), fatigue (72%), menstruation (36% of women), alcohol (30%), cold or hot weather (27%), missing a meal (24%), weekend (13%), overeating (12%), and food (7%). The most frequently reported trigger factors for TTH were stress (77%), fatigue (62%), missing a meal (20%), cold or hot weather (18%), alcohol (17%), menstruation (11% of women), overeating (8%), weekend (5%), and food (5%). Beck depression inventory score was not different between migraine (22.0 ± 4.8) and TTH (23.4 ± 5.8).

Conclusions: Stress and fatigue were most frequent triggering factors for both headache types. Prevalence of depression and unilaterality of headache is not different between two groups.

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Headache epidemiology and outcomes

Transition from episodic to chronic migraine and relationship with pain comorbidity: results from the cameo (chronic migraine epidemiology & outcomes) study

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Background: Chronic migraine (CM) is associated with comorbid medical conditions, including chronic pain.

Aim: To determine whether pain comorbidity predicts the transition from episodic migraine (EM) to CM after 3 months.

Method: Participants were recruited from an Internet-based research panel using quota sampling, and Web-based questionnaires were completed at baseline and 3 months. US-based respondents who met modified *ICHD-3 beta* criteria for migraine were classified as having EM (<15 headache days/month) or CM (≥ 15 headache days/month). The validated, 5-point Total Pain Index was used to assess the frequency of pain (0 [none of the time] to 4 [all of the time]) in 8 body regions (excluding the head). Multivariate binary logistic regression was used to assess the influence of the number of extra-cephalic pain sites (EPS) occurring most or all of the time on the transition from EM to CM and/or the maintenance of CM (EM = reference group).

Results: Of 8,908 eligible respondents, 8,139 (91.4%) had EM and 769 (8.6%) had CM at baseline. After 3 months, 278 (3.4%) respondents with baseline EM transitioned to CM; 385 (50.1%) baseline CM respondents remained CM. In unadjusted models, the odds of transitioning from baseline EM to CM increased 43% with each EPS; for

Table. Increased Odds of CM with Each Additional EPS

Baseline HA Status (Result)	Unadjusted OR (95% CI)	Adjusted for Demographics OR (95% CI)	Adjusted for Demographics and Baseline HA Frequency OR (95% CI)
EM (Transition to CM)	1.43 (1.33, 1.53)	1.42 (1.33, 1.52)	1.30 (1.21, 1.40)
CM (Remain CM)	1.16 (1.08, 1.25)	1.15 (1.07, 1.25)	1.06 (0.97, 1.16)

CI=confidence interval; CM=chronic migraine; EM=episodic migraine; EPS=extra-cephalic pain site; HA=headache; OR=odds ratio.

participants with baseline CM, the odds of maintaining CM increased 16% with each EPS. Results for adjusted models are shown in the **Table**.

Conclusion: A high propensity for extra-cephalic pain is associated with (1) progression from EM to CM and (2) maintaining CM at 3 months post-baseline.

Funding: Allergan, Inc.

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Headache epidemiology and outcomes

Clinical profile of headache at the emergency department in a low income population

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Background: Headache is a common complaint of patients presenting to the emergency department (ED).

Aim: Analyze and classify the clinical features of headache at the ED in a low income population of Bogota-Colombia

Methods: We conducted an observational, descriptive, and cross-sectional study from January to December of 2012. The data for all patients with headache, attending the ED at the Kennedy Western Hospital in Bogotá-Colombia were prospectively registered. Diagnosis of headache was according to the International classification of headache disorders, 2nd edition (ICHD-II).

Results: A total of 667 patients out of 1,898 consulted for headache (35.1%); 32.2% patients were classified as having primary headache, and 67.8% as secondary headache. The mean time prior to consult was 11.3 days in both groups. For primary headache, 27.1% had migraine. In the group of secondary headache de most frequent diagnosis were: headache attributed to infection (16,7%); headache attributed to cranial or cervical vascular disorder (16,1%) and headache attributed to non-vascular intracranial disorder (12,8%). Patients with primary headache suffered a more severe headache (intensity) (p: 0,002), and were younger (p: 0, 0005) than patients with secondary headache. Non patients with secondary headache had osmophobia. The most common alarm signs were: coexisting systemic disorders, headache onset before the age of 50 years and history of immunosuppression.

Conclusion: In low income populations, headache is one of the main reasons for emergency room visits, and apparently, secondary headaches are more common. In this population, the semiological profile is useful for the clinical approach and the differential diagnosis.

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Headache epidemiology and outcomes

Semiological profile of headache attributed to cranial vascular disorders

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Background: Headache is common and in some opportunities the unique symptom of a cranial vascular disorder. Semiology is important to guide an opportune diagnosis and treatment.

Aim: Describe the clinical profile of headache attributed to cranial vascular disorders at the Emergency Department.

Methods: We conducted an observational, descriptive, and cross-sectional study from January to December of 2013. The data for all patients with headache, attending the ED at the Kennedy Western Hospital in Bogotá-Colombia were prospectively registered. Diagnosis of headache was according to the International classification of headache disorders, 3th edition (ICHD-3 Beta).

Results: Headache attributed to cranial vascular disorder accounted for 16% (n = 108) of all patients with headache attending the emergency department of neurology. The most frequent diagnoses were: Headache attributed to ischaemic stroke (43,5%); Headache attributed to cerebral

venous thrombosis (CVT) (23%); Headache attributed to transient ischaemic attack (TIA) (13,8%) and Headache attributed to non-traumatic subarachnoid haemorrhage (SAH) (10%). Thirty percent of patients had a migraine-like pattern. The group of patients with headache attributed to cerebral venous thrombosis were the only ones who presented with autonomic features (8%).

Conclusion: Headache attributed to cranial vascular disorder is common in our population. Migraine-like pattern was the most frequent clinical profile in these patients. It is still to be determined if some clinical characteristics such as autonomic symptoms, may be useful in the differential diagnosis of headache attributed to cranial vascular disorders, particularly in cerebral venous thrombosis.

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Headache epidemiology and outcomes

Migraine-type headache in Armenia

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Background: The prevalenceof migraine headache varies betweendifferent geographical regions. This study was designed toestimate the 1-year prevalence of migraine and identify theirdemographic characteristics of participant.

Methods: We investigatedthe prevalence of migraine in a population-basedsample in Armenia. A total of 141 subjects aged between 18 and 78 years were screened fromOctober 2011 until September 2013 in a door-to-door survey using aquestionnaire. Migraine diagnoses were based onInternational Headache Society Classification.

Results: Out of 141participants (mean age 36.2 ± 12.8 years; 52.5%women) about half of them reported recurrent headaches and24 were diagnosed with migraine at a prevalence rateof 17.02% (10.3% in men and 23.1% in women). Therate of migraine with aura among migraineurs was 31%. Theprevalence of migraine was highest (36.4%) among 28 to 40-year-oldparticipants and then it declined after 40 yearsof age. More than 2/3 of migraineurs (64.2%) had consulted aphysician whereas 1/3 of them had never consulted one.A majority of patients (77%) complained of moderate orsevere headaches. The most common precipitatingfactors were mental stress, lack of sleep and not eating ontime (87.2%, 68.6%, and 37.8%, respectively).

Conclusion: The studydemonstrated a high prevalence of migraine inadults. The one-year prevalence of migraine estimated as16.7% was similar to a nationwide home-based Armenian studyand higher than previous studies conducted in other Caucasiancountries. Furthermore, it was not lower than in European countries and identical to a previous nation-wide study conducted in USA.

PO299

Headache epidemiology and outcomes

The impact of chronic migraine on the quality of life and on the national health system in patients attending an Italian 3rd level headache centre

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Background: Chronic migraine (CM) has a high impact on functional performance and quality of life (QoL). CM also has a relevant burden on the National Health Service (NHS), however precise figures are lacking.

Aim: To evaluate the impact of CM on functional capability and QoL on sufferers, as well as its economic impact on the national health system (NHS) in a representative cohort.

Methods: We enrolled 92 consecutive patients:51 subjects with CM and 41 with episodic migraine (EM). Patients were tested with disability scales (MIDAS, HIT-6, SF-36) and with an *ad hoc* semi-structured questionnaire.

Results: CM subjects had scores higher than EM for MIDAS (98.4 ± 72,3 vs 15.5 ± 17.7, $p = 0.001$) and for HIT-6 (66.1 ± 8.4 vs 58.7 ± 10.1, $p = 0.001$). The SF-36 score was 39.9 ± 14,74 for CM and 66.2 ± 18.2 for EM ($p = 0.001$).

For CM, the direct mean annual cost (in euro) per patient was 2250 ± 1796.1, against 523.6 ± 825.8 per patient with EM. The cost loaded on NHS was 2110.4 ± 1756.9 for CM, 468.3 ± 801.8 for EM. The total economic load and the different subitems, were significantly different between groups (CM vs. EM $p = 0.001$ for each value).

Conclusions: CM is a disabling condition with a huge impact on the QoL of sufferers and a significant economic impact on the NHS. The adequate management of CM, reverting it back to EM, will provide a dual benefit: on the individual and on the society.

PO300

Headache epidemiology and outcomes

Prevalence and knowledge of headaches among Japanese hospital workers

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Studies of the prevalence of headaches inhospital workers are scant. Therefore, we investigated the incidence andknowledge regarding preventive drugs and medication overuse for headaches amongall workers at our hospital. We sent original questionnaires to all 532 workersat our hospital. In total, 386 (72.6%) valid questionnaires were analyzed.

Headaches were present in 219 (56.7%) subjectsand severe headaches were present in 77 (19.9%) subjects. A female sex was identifiedto be a significant risk factor for headaches, whereas the type of job of thehospital worker was not. In addition, the frequency of severe headaches washigh in the subjects in their thirties. Only 70 (32.4%) of the 219 headachesufferers had visited a clinic for treatment; the most frequently visiteddepartment was the department of neurosurgery. Among the 219 headache sufferers,171 (80.7%) were unaware of preventive medications for headaches, and 155 (73.5)did not have knowledge regarding the overuse of medications for headaches, despiteworking in a hospital. Japanese hospital workers frequently suffer from headaches,more so than the Japanese general population. A female sex is a significantrisk factor for headaches, and the rate of severe headaches is high amongindividuals in their thirties. Most headache sufferers are unaware of proper preventivemedications for headaches and the potential for medication overuse, evenworking at a hospital. Public education for both patients and the generalpopulation as well as hospital workers is therefore necessary to reduce theincidence of headaches and inappropriate use of medications.

PO301

Headache epidemiology and outcomes

Vestibular migraine in Korea : an application of the ICHD-3 beta diagnostic criteria

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Background: Vestibular migraine (VM) accepted in an appendix of the third edition of the International Classification of Headache Disorders as a first step for new entities. Thus, to assess the epidemiology of vestibular migraine based on ICHD-3 beta, we conducted a prospective multi-center outpatient clinics study in Korea.

Methods: Nine neurologists from university or regional hospitals enrolled consecutive first-visit patients for headache. The classification of headache disorder was done by each investigator according to ICHD-3 beta, or by a consensus meeting for the uncertain cases. After diagnosis of current headache, the history about VM was separately assessed. The clinical characteristics of patients diagnosed as VM were assessed and compared to who fit the criteria of migraine but not the criteria of VM (NVM).

Results: Of the 426 patients with migraine assessed, 50 patients were assigned to VM (11.7%). The mean age of patients with VM 42.6 years and 76% of patients was female. Distribution of accompanied migraine diagnosis according to by ICHD-3 beta were chronic migraine (14.5%) followed by migraine without aura (12.3%), and migraine with aura (9.4%). The most common symptoms that qualify for a diagnosis of VM were: spontaneous vertigo (34.5%), positional vertigo (25.9%), head motion-induced dizziness with nausea (22.4%), etc and mean

duration of episodes were 402 minutes (±784.9). The Clinical and headache characteristics did not differ significantly between patients with VM and with NVM.

Conclusions: This study provides data on the prevalence of the new diagnostic entity of VM, and its clinical characteristics in Korea.

PO302

Headache epidemiology and outcomes

Clinical application of the international classification of headache disorders, 3rd edition, beta version in first-visit patients for headache: a multi-center outpatient clinics study in Korea

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Background: The International Classification of Headache Disorders has been revised as its 3rd edition, beta (ICHD-IIIβ). The clinical application in practice is needed to test the feasibility and usefulness of ICHD-IIIβ.

Methods: Eleven neurologists from tertiary hospitals enrolled consecutive first-visit patients for headache from August to December 2014. The classification of headache disorder was done according to ICHD-IIIβ by each investigator based on the initial evaluation or by a consensus meeting for the difficult cases. The characteristics of headaches were analyzed and the feasibility and usefulness was assessed by the proportion of unclassified headache disorders using ICHD-IIIβ compared to the previous version.

Results: A total of 1141 patients were enrolled with the mean age of 47.4 ± 14.7 years and the female/male ratio 1.76:1. Primary headache disorders were diagnosed in 1007 patients (88.3%): 489 migraines, 307 tension-type headaches, 16 cluster headaches, and 195 other primary headache disorders. One hundred one patients (8.9%) had secondary headache disorders or painful cranial neuropathies/other facial pain and 33 patients (2.9%) could not be classified by ICHD-IIIβ. The main reasons to be unclassified were insufficient fulfillment, unfinished check-up, and absence of suitable classification. The diagnoses differed as compared to the previous version in 159 patients (13.9%): 12.6% differed due to the mitigation of the previous strict criteria and 1.3% differed due to the introduction of a new diagnostic category.

Conclusions: Classifications by ICHD-IIIβ are possible in more than 97% of the first–visit headache patients and ICHD-IIIβ has proved to be more useful than its previous version.

PO303

Headache epidemiology and outcomes

Trend of patients at a headache clinic

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Background: Headache clinics became popular in Japan, but we do not know whether patients are treated appropriately, and are satisfied.

Aim: An aim is to comprehend status of revisit at a headache clinic.

Method: A series of 100 patients (28men, 72women, 46 years) who visited our headache clinic for the first time were recruited. Clinical information was obtained from medical records. A status of visit at one year after the first visit was decided in three following categories: 'visit-regularly', 'completed', 'dropout'. Correlation between status of visit and clinical information was evaluated.

Results: Sixty-seven of 100 patients were migraineurs. Sixteen of 67 migraineurs had another headache. A status of visit were decided as 'visit-regularly' in 40, 'completed' in 39, 'dropout' in 21. The visit number of times until 'completed' was an average of 1.8 (a median 1). The visit number of times until 'dropout' was an average of 2.2 (a median 1). The ratio of 'visit-regularly' was higher in women (47%) than in men (21%), and was significantly higher in migraineurs (52%) than in non-migraineurs

(15%). In migraineurs, patients who were decided as 'visit-regularly' recorded more frequent headache attacks than patients who were decided as 'completed', used less pain-killers than patients who were decided as 'dropout'. There were no relationships between status of visit and age, prescription, comorbidity.

Conclusion: Most of patients at the headache clinic were migraineurs and 40% of them visited regularly. To avoid dropout and to treat patients appropriately, the first visit is the most important as a specialist.

PO304

Headache epidemiology and outcomes

Prevalence of restless leg (RLS) syndrome and association of chronic migraine and obesity in a Japan regional headache center

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Background and Aim: Cornification of migraine is urgent issues in Japan as well as Western countries. To survey possible association of RLS, obesity and headache cornification.

Subjects and Methods: In a Japanese regional headache center, we prospectively surveyed 4909 headache suffers, including 2776 migraineurs, 1346 subjects with tension-type headache(TTH), 247 with trigeminal autonomic cephalalgia (TACs) and 540 with the other miscellaneous headaches (Msc), since 2012.

The diagnosis of headaches were established in accordance with ICHD-2 or 3beta, following full neurological examinations and appropriate examinations. RLS were diagnosed by the International RLS Study Group criteria. Body mass index (BMI) was calculated and categorized with WHO system.

Results: Prevalence of RLS at the first visit were 14.5% in migraine, 10.8% in TTH, 8.9% in TACs, and 7.2% in Msc. Prevalence of RLS in migraine was significantly higher than in TTH, TACs and Msc (Pearson's chai-square test, $p < 0.001$). Prevalence's of chronic migraine (CM) were significantly high in overweight group ($BMI > 25$) and obesed groups ($BMI > 30$). Mean ($\pm$SE) migraine days were 7.4 ± 0.3, 7.4 ± 0.1, 8.7 ± 0.6, 9.7 ± 0.9, and 10.8 ± 1.5 in underweight, normal, overweight, obese, and morbid obese migraineurs, respectively. Prevalence of chronic TTH did not significantly correlate with BMI. Mean migraine days were 7.9 ± 0.2 days in migraineurs with RLS and 7.8 ± 0.4 days in migraineurs without RLS (N.S).

Conclusion: Obesity is correlated with cornification of migraine but TTH in a Japanese large series. RLS is prevalent in migraineurs, however, did not associated with migraine cornification.

PO305

Headache epidemiology and outcomes

Migraine burden on migraineurs and their spouses/domestic partners: results from the cameo (chronic migraine epidemiology & outcomes) study

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Background: Despite advances in our understanding of migraine, much is still unknown about the burden it places on the family.

Aim: Migraineur (proband) and partner reports from CaMEO were used to explore familial migraine burden.

Method: US respondents meeting modified *ICHD-3b* criteria for migraine were classified as having episodic migraine (<15 headache days/month) or chronic migraine (CM; $\geq$15 headache days/month). Participants and their spouses/domestic partners completed Web-based questionnaires assessing migraine-related family burden. Survey items were selected using exploratory and confirmatory factor analysis models. Analyses examined proband and partner item endorsement rates as a function of headache frequency.

Results: 4,022 proband-partner dyads were included. The mean (SD) age for probands was 43.2 (13.5) years, and for partners was 44.5 (13.9) years; most probands were female (73.3%), and most partners were male (72.9%). Exploratory and confirmatory factor analyses, along with expert clinical input, identified 19 items within 4 domains: (1) reduced participation/enjoyment, (2) missed/canceled events, (3) financial impact, and (4) partner interactions. Migraineurs and partners demonstrated burden across all headache frequencies, with generally greater burden for migraineurs than partners and increasing burden with

Table 1. Migraineur-Partner Reduced Activity Participation/ Enjoyment as a Function of Migraine Frequency Status

	Migraineur				Partner			
	EM			CM	EM			CM
	0-4 HA	5-9 HA	10-14 HA	≥15 HA	0-4 HA	5-9 HA	10-14 HA	≥15 HA
Item	Participation/Enjoyment Burden[1] (≥1 day past 30d), %							
Did not participate in a family activity at home	37.3	65.6	71.9	77.3	22.3	41.1	40.9	50.7
Did not do anything 'physical' with family	37.1	62.2	69.1	76.1	19.5	38.1	44.4	53.1
Involvement/enjoyment in family activity was significantly reduced	39.9	70.7	79.1	85.9	23.2	46.3	52.4	62.3
Participation/enjoyment in an important celebration/event was significantly reduced *(past year)*	37.6	67.9	71.4	79.2	22.0	40.4	45.5	51.0
One-on-one time with partner was disrupted	40.3	67.2	71.3	76.8	43.7	68.5	68.9	77.2
Partner had to take over migraineur's share of housework	39.3	67.4	70.7	77.7	41.3	62.4	67.6	73.4
Enjoyment of time spent with partner was significantly reduced	43.9	76.3	82.9	86.1	40.8	65.1	70.7	76.5

CM=chronic migraine; EM=episodic migraine; HA=headache.
[1]These items refer to burden as a function of the migraineur's headache.

Table 2. Migraineur-Partner Missed/Canceled Events and Financial Burden as a Function of Migraine Frequency Status

	Migraineur				Partner			
	EM			CM	EM			CM
	0-4 HA	5-9 HA	10-14 HA	≥15 HA	0-4 HA	5-9 HA	10-14 HA	≥15 HA
Item	Missed/Canceled Event Burden[1] (≥1 day past year), %							
Missed a holiday or religious celebration	10.7	27.4	33.2	40.8	10.3	20.6	26.1	26.4
Missed a wedding, graduation, retirement celebration or other event important to you	10.3	24.5	24.6	39.0	8.0	17.1	25.5	29.0
Canceled an important celebration in your home because of migraineur's headache	9.0	23.2	28.3	38.1	8.8	21.2	27.0	31.7
	Financial Burden[1] (Agree Somewhat/Completely), %							
I worry more about covering the household expenses	22.0	38.7	42.3	54.9	13.2	21.9	24.0	33.8
I worry about having long-term financial security for me/my family	25.1	42.7	44.3	59.5	15.8	26.3	29.6	40.4
I worry about losing my job or being laid off (if employed)	17.1	31.3	39.3	44.8	9.4	15.6	15.1	25.0
It has been harder for partner to advance in his/her job (item asks about partner's job advancement from both migraineur and partner perspective)	10.1	18.5	19.1	23.5	6.6	11.9	13.2	15.5

CM=chronic migraine; EM=episodic migraine; HA=headache.
[1]These items refer to burden as a function of the migraineur's headache.

Table 3. Effect on Migraineur-Partner Interaction as a Function of Migraine Frequency Status

	Migraineur				Partner			
	EM			CM	EM			CM
	0-4 HA	5-9 HA	10-14 HA	≥15 HA	0-4 HA	5-9 HA	10-14 HA	≥15 HA
Item	Interaction Burden[1] (Agree Somewhat/Completely), %							
Partner does not really believe migraineur about headaches	24.4	37.0	40.4	43.9	14.0	17.8	22.6	22.1
Partner gets upset or angry at migraineur for having headaches	9.4	19.6	22.6	27.5	12.1	22.8	25.0	26.7
Partner avoids migraineur at time because of headaches	17.2	31.6	32.1	39.5	27.6	33.9	36.8	45.5
Partner resents having to do everything when migraineur has a headache	12.8	22.6	24.4	28.8	10.6	17.0	15.7	23.4
Migraineur's headaches cause stress in relationship even when migraineur does not have a headache	9.9	20.7	26.0	37.4	9.7	20.1	21.5	30.7

CM=chronic migraine; EM=episodic migraine; HA=headache.
[1]These items refer to burden as a function of the migraineur's headache.

increased headache frequency across all domains **(Tables 1–3)**.

Conclusion: Results offer a unique view into migraine burden, as data were collected from both the migraineur's and partner's perspectives. Migraine burden is significant and pervasive. Each domain showed impact for both migraineurs and their partners across every headache frequency group. Not surprisingly, burden was greatest among those with CM and their partners.

Funding: Allergan.

PO306

Headache epidemiology and outcomes

Comorbid pain syndromes in migraine

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Several large studies have characterized selected pain syndromes (PS) comorbid to various types of headaches. The aim of our study was to describe comorbid chronic PS in episodic (EM) and chronic migraine (CM).

Methods: We recruited 103 patients with migraine defined by ICHD 3rd edition: 71 patients with CM and

32 with EM. Pain syndromes were diagnosed using a questionnaire.

Results: The structure of chronic PS in migraine was as follows: 33% of patients had no comorbid PS; 26.5% of patients had at least 1 PS; 2 and more PS were found in 36.9% of patients. The following PS were most prevalent: neck pain (35.9%), low back pain (31.1%), arthralgia (16.5%), abdominal pain (14.5%), and leg pain (8.7%). Prevalence of temporomandibular joint disfunction (TMD) was 41.7%.

In patients with rare EM (<4 migraine days/month) we found less PS compared to patients with frequent EM (5–14 migraine days/month) or CM: neck pain 0% vs. 43% ($p = 0.009$), low back pain 11.7% vs. 34.9% ($p = 0.023$), arthralgia 0% vs. 19.7%% ($p = 0.04$), abdominal pain 0% vs. 17.4%($p = 0.006$), leg pain 0% vs. 10.5% ($p = 0.005$), pain in the arms 0% vs. 9.3%, TMD 26.1% vs. 46.2% ($p = 0.001$).

We found no correlation between the number of comorbid PS and duration of migraine (EM or CM).

Conclusions: Comorbid PS are present in two thirds of patients with migraine. Neck pain, low back pain, and TMD are the most prevalent PS in migraine. Prevalence of comorbid PS is higher with increasing frequency of migraine.

PO307

Headache epidemiology and outcomes

Comparison of hit-6 questionnaires in patients addressed to neurologist versus persons revealed by filling of questionnaires

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Background: Primary headaches like tension type (TTH) and migraine (M) are very common among population. The prevalence of TTH is about 70 %, of migraine 10–15%. In more cases of TTH and M, especially in chronic and mixed cases they have substantial impact on quality of life.

Aim of study was comparison of scores of HIT-6 between patients addressed to neurologist and persons who whenever had headache and was revealed by filling of questionnaires blindly distributed among them.

Methods: Questionnaires on screening of headaches (according to recommendations of International Headache Society) and HIT-6 were filled by 1000 person (759 women/241 men) from which 500 (383 females/117 males) addressed to neurologist and 500 (376 female/124 males) revealed by filling of questionnaires. Age of participants was 42 ± 16 years.

Results: Data analysis revealed that in 500 persons addressed to neurologist 276 had very severe, 98 substantial and 126 some impact on their life because of headache. In group revealed by filling of questionnaires 42 had substantial, 121 some and 337 little to no impact on their life. In more cases of very severe impact in both groups was revealed coincidence of TTH and M with and without aura and chronic forms of TTH and M and scores are 65 ± 5 but in first group scores range from 64 to 70 and in second one from 60 to 65.

Conclusion: Our data proves that patients with chronic TTH and M and/or combination of TTH with M had lower quality of life and suffers more.

PO308

Headache epidemiology and outcomes

Migraine in modern Kyrgyzstan

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Migraine in modern Kyrgyzstan

Background: Adequate diagnosis and treatment of migraine is a relevant problem in modern Kyrgyzstan. A group of 22 patients was examined to determine prevalence and clinical features of migraine, based on multidisciplinary approach in diagnosis and treatment.

Aim: etiological factors and clinical picture of classic and associated migraine research.

Methods: 22 patients: 18 females and 4 males were examined in Neurology department, National Hospital. Paraclinical research: electroencephalography, rheoencephalography, ophthalmologist's examination, duplex scanning of cervix blood vessels, brain blood vessels and cervical spine MRI.

Results: Simple form of migraine was detected in 59%. In 87% pain was localized in one half of the head, and then 13% cases indicate transfer to the other half. 92% indicated right-handed pains, and only 8% left-handed. Most of the

patients had attacks developed during day time, with following vegetative changes. Average duration of migraine without aura is 1 to 24 hours. Attacks rate – 2 to 4 times a month.

Migraines aura was detected in 13.5% cases. Ophthalmic aura – 2%. We have also observed severe basilar or syncope migraine.

Instrumental examination with simple form migraine identified nonspecific changes. Associated migraine combines with blood vessels anomaly. 27.5% have migraine developed due to vertex vertebral pathology.

Conclusion: 1. Simple migraine is a common compensated form of migraine without cerebral blood vessel inbred morphological changes.

2. Associated migraine features more severe course, combined with cerebral arteries development anomaly and requires different tactics, which would involve angiosurgeon, due to risk of migraine stroke development.

PO309

Headache epidemiology and outcomes

The development of a self-efficacy scale for chronic headache: a preliminary study

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Background: Self-efficacy is a situation specific sense of self-confidence that one can perform needed actions to achieve desirable or avoid undesirable outcomes. Self-efficacy is important to assess in persons with chronic headache due to the need for self-management strategies. Currently, evaluation of self-efficacy in this population is lacking.

Aim: The purpose of this study is to develop a *multifaceted* Self-Efficacy Scale, to provide more insight into the dynamics of self-management behavior as it pertains to chronic headache.

Methods: Our goal was to determine what domains are meaningful to patients with chronic headache in order to develop a scale of no more than 15 questions.

The scale was developed from:

1) Polling a multi-disciplinary team involved in the management of patients with chronic headache. This team is comprised of: two neurologists, two physical therapists, one occupational therapist, one nurse practitioner and two pain psychologists.

2) An open-ended survey sent to a retrospective sample of patients referred to USC Physical Therapy Associates for treatment of chronic headache.

Results: A preliminary questionnaire was developed that has 13 items divided into two dimensions, headache management and activity performance. Items were included based on frequency of responses given by the sample of patients as well as feedback from the multi-disciplinary team.

Conclusion: The Chronic Headache Self-efficacy Scale (CHASE) is a multifaceted measure that will assist in identifying meaningful self-management areas where patients would benefit from further educational interventions. CHASE requires validation.

PO310

Headache epidemiology and outcomes

Which test to use to measure migraine's burden and influence on everyday life?

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Background: Migraine is a debilitating disorder. There are numerous questionnaires aimed to measure migraine's burden and influence on persons' health related quality of life (HRQoL).

Aim: The aim of this study was to compare results provided from the usage of questionnaires primarily designed to be more or less migraine/headache specific with generic ones, based on what practical recommendations for test-selection could be provided.

Methods: This is a non-randomized prospective cross-sectional study. Three questionnaires available and validated in Estonian were used. HRQoL was measured with the self-administered RAND 36-item Health Survey (RAND-36). To evaluate the impact headaches have on the ability to function Headache Impact Test (HIT-6) was used. To determine how severely migraine affects patients' life Migraine Disability Assessment Test (MIDAS) was selected. The study was approved by the Research Ethics Committee of Tartu University.

Results: One hundred and five consecutive consented migraine patients, who visited the Headache Clinic of Tartu University Clinics for consultation, filled in the questionnaires. The RAND-36 control group consisted of 176 individuals from the Estonian population, matched by age and sex. Results from RAND-36 were statistically significantly different between migraine patients and controls (the p-value ranged from $<2.2\,e^{-16}$ to 0.03), except for the general health domain ($p = 0.74$). RAND-36 results correlated with HIT-6 and more strongly with MIDAS scores.

Conclusion: Since RAND-36 scores correlate with HIT-6 and MIDAS ones, considering the fact that generic HRQoL tests are more time-consuming, the practical suggestion would be to use more migraine specific tests in everyday clinical practice.

PO311

Headache epidemiology and outcomes

Evaluation of postoperative change in quality of life in patients with trigeminal neuralgia

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Background: Trigeminal neuralgia (TN) is a disorder that can cause excruciating pain and diminish quality of life (QoL).

Aim: The aim of this study was to comparatively evaluate the efficacy of microvascular decompression (MVD) and percutaneous retrogasserian glycerol rhizotomy (PRGR) for the treatment of TN and measure treatments' influence on QoL.

Method: This is a retrospective nation-wide cohort study. All reachable and consented patients treated with MVD or PRGR in Estonia between 2002 and 2013 filled in Headache Impact Test 6 (HIT-6), Emotional State Questionnaire 2 (ESQ-2), numeric rating scale (NRS) and specifically designed questionnaire to measure the TN related outcomes before and after the treatment. This study was approved by the Ethics Review Committee on Human Research of the University of Tartu.

Results: Seventy nine out of 127 operated patients replied (response rate = 62.2%). The MVD group consisted of 43 and the PRGR of 50 procedures (5 patients underwent both treatments). The mean age of responders was 59 (31–79; SD ± 13) in the MVD and 66 (41–84; SD ± 10) in the PRGR group. NRS mean scores dropped from 9.1 to 1.7 for MVD and from 8.3 to 3.2 with PRGR. Problems with eating and/or speaking disappeared in 66.7% after MVD and in 26.3% after PRGR. However the results of ESQ-2 and HIT-6 did not differ significantly.

Conclusion: Both methods are effective in the treatment of trigeminal neuralgia, but MVD is the preferred one in the majority of the cases.

PO312

Headache epidemiology and outcomes

Association of headache prevalance with early menarche in female medical students

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Background: Hormonal events in women is suggested to be associated with headache onset, severity, frequency and chronicity.

Aim: To investigate the relationship between menarche age, headache prevalence and onset of primary headaches.

Material and Method: 427 female students, whom invited to participate the study answered the questionnaire. All of them answered a questionnaire about their headache, sociodemographic features and hormonal status. 311 of them who complained about headache, responded a second questionnaire.

Results: Of those who took the second questionnaire, 118 diagnosed as migraine and 193 tension type headache. We found that elder menarche onset was associated with elder headach onset ($p < 0,05$). There was no relationship between headache prevalence and menarche age in both headache groups. However, chronic migraine (CM) prevalence and menarche age is significantly related ($p < 0,05$). The average age at menarche was found younger in CM (12 years) as compared to other subgroups (13 years) ($p < 0,05$). There is also a relation between oral contraceptive intake and headache frequency and less headache complaints ($p < 0,05$). Participants with higher body mass index were younger at menarche and experienced increased headache severity ($p < 0,05$).

Conclusion: These findings suggest a possible relationship between headache and menarche age. This relationship might be due to the effects of ovarian hormones on

the central nervous system. Our findings should be supported wider population based studies.

PO313

Headache epidemiology and outcomes

Comorbidity of gastrointestinal disorders and migraine

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Background: Previous studies have shown that migraine headache is impacted by gastrointestinal issues. However few studies assessed the relationship of headache and gastrointestinal disorders.

Aim: In the current study we aimed to evaluate the relationship between migraine and different lower and upper gastrointestinal disorders as well as non-alcoholic fatty liver and cholelitiasis in overweight and obese adults.

Methods: 1622 consecutive overweight and obese individuals (267 men and 1355 women) were enrolled in this cross-sectional study. Migraine was diagnosed according to International Headache Classification Disorder-II diagnostic criteria. Constipation was diagnosed according to Rome III criteria and patient's report. Dyspepsia was diagnosed based on patient's complain about epigastric pain and discomfort. The diagnosis of Irritable bowel syndrome (IBS) was based on gastrointestinologist's report. The diagnosis of fatty liver, and cholelitiasis was based on abdominal ultrasonographic findings.

Results: From recruited patients 182 individuals were suffered from migraine headache. Constipation (11% in migraineurs vs 3.1% in controls, $P < 0.0001$), dyspepsia (18.7% in migraineurs vs 4.5 % in controls, $P < 0.0001$), heartburn (7.1% in migraineurs vs 1.5% in controls, $P < 0.0001$) and IBS (4.4% in migraineurs vs 0.9% in controls, $P = 0.001$) were significantly more prevalent among migraineurs. No significant relationship was observed between migraine and cholelitiasis or fatty liver.

Conclusion: Our results showed that upper and lower gastrointestinal disorders are more prevalent in migraineurs and the question rise whether gastrointestinal disorders provoke migraine.

PO314

Headache epidemiology and outcomes

Clinical correlates of migraine in mood disorders

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Background: A relationship between migraine and mood disorders has been well established. However, differences in clinical correlates among the specific mood disorders of bipolar type I, type II and major depression has been less evaluated.

Aim: To examine the association between migraine and clinical correlates in bipolar disorder types I and II and major depression.

Methods: 186 participants were recruited from the Mood Disorders Program of the McGill University Health Center in Montreal, Canada. Data was gathered using structured diagnostic interviews (SCID) and medical chart reviews. A questionnaire based on the diagnostic criteria published by the International Headache Society (IHS) was used to obtain migraine information. Chi-square analyses and t-tests were conducted to examine the association between migraine and clinical correlates.

Results: Females ($p = .039$) and participants with Bipolar type II vs. I ($p = .025$) met more criteria for migraine diagnosis. Family history of migraine was associated with meeting more criteria ($p = .000$), and meeting full criteria ($p = .016$) for migraine diagnosis. Migraine diagnosis was associated with more psychiatric comorbidities ($p = .020$), and fewer psychiatric hospitalizations ($p = .024$).

Conclusions: Being female, bipolar type II and family history of migraine were associated with meeting more criteria for migraine diagnosis. The greater comorbidity found in the migraine group supports the importance of screening for comorbidities in these populations. Mood disorder patients with a migraine diagnosis had fewer psychiatric hospitalizations. This finding should be investigated to determine if factors such as increased help-seeking behavior in patients with migraine affect such outcomes.

PO315

Headache epidemiology and outcomes

The feasibility, cost-effectiveness, and clinical efficacy of a headache clinic run by a general practitioner (GP) with a special interest in headache, outside of a hospital setting

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Background: Primary headaches are amongst the most prevalent and burdensome disorders in the world. The availability of headache services is disproportionately small. In the UK, patients with headache are usually managed by Neurologists in a hospital outpatient department (OPD), which is both expensive and stretches their capacity.

Aim: To assess the feasibility, cost-effectiveness, and clinical efficacy of a headache clinic run by a General Practitioner (GP) with a special interest in Headache, outside of a hospital setting.

Methods: Patients due to be seen in the local OPD were given the option to attend a GP-lead community clinic instead. Baseline data was obtained on the burden of their headache, and the extent to which they felt able to manage their headache (a measure of self-perceived autonomy). Perceived autonomy and patient satisfaction were assessed immediately after their consultation, and the burden of headache assessed approximately 3-months later. Other outcomes measured were the proportion of patients requiring imaging, the proportion discharged, and running costs per head.

Results: Data points were obtained on 56 patients. Compared to the OPD, the community clinic incurred 33% less cost; 26.8% required imaging (vs. 67%); 73.5% were discharged (vs. approximately 40%). Patients felt significantly more empowered their headache after the consultation ($t_{(100)} = 6.938$, $p < 0.0001$). Patient satisfaction was extremely high. Three-month follow-up data is awaited.

Conclusion: A community headache clinic runs at two-thirds cost, makes less than half the imaging requests, and has half the follow-up rate, when compared to OPDs. High patient empowerment and satisfaction scores are achievable.

PO316

Headache epidemiology and outcomes

Headache in relapse and remission phase of multiple sclerosis

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Background: People with multiple sclerosis (MS) have an increased incidence of headaches, although the comorbidity of headaches and MS is poorly understood.

Aim: We aimed to compare the prevalence of headache in MS patients and normal population. Also assess whether headache could be a presenting symptom of MS attack.

Methods: Sixty five MS patients and 65 matched controls were enrolled in current case-control study. Different headache types were diagnosed according to International Headache Classification Disorder-II diagnostic criteria. Intensity, frequency, and duration of headache attacks were also assessed.

Results: 27.7% (18 persons) of controls were suffered from headache. In contrast, 40% (26 individuals) and 38.6% (22 individuals) of MS patients experienced headache in relapse and remission phase respectively. The risk of headache was significantly higher among MS patients (OR: 2.9, P. Value: 0.006).

In MS patients who experienced headache during attacks, 8 (30.7%), 14 (53.8%), and 4(15.3%) were suffered from tension, migraine and secondary headache respectively. Among them symptoms related to cerebral, brain stem, spinal cord, and optic nerve involvement were observed in 38.4%, 15.3%, 15.3%, and 23.7% respectively. No significant difference was observed between the type of attack and headache type. No significant difference in intensity, frequency, and duration of headache was observed between relapse and remission phase.

Conclusion: The risk of headache was significantly higher in MS patients. According to the current results headache could not be assumed as a presenting symptom for MS attack.

PO317

Headache epidemiology and outcomes

Comorbidity of eating disorders in individuals with mood disorders and migraine

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Background: The relationship between migraine and mood disorders has been well established. Early reports now suggest migraine may be risk factor for eating disorders[NCL1]. But it remains unknown whether migraine among mood disorders is also associated with eating disorders. Multiple comorbidities are associated with higher healthcare utilization and greater impairment.

Aim: To examine the association between migraine diagnosis and eating disorders within a mood disorder sample.

Method: One hundred fifty three (153) participants were recruited from the Mood Disorders Program of the McGill University Health Center in Montreal, Canada. Data was gathered using a structured diagnostic psychiatric interview for DSM-IV (SCID) and medical chart review. Migraine was gathered using a clinician-administered questionnaire based on the IHS criteria (1988). Chi-square analyses were conducted to examine the association between migraine diagnosis and eating disorders.

Results: Diagnosis of migraine was associated with diagnosis of an eating disorder ($\chi^2(1, N = 153) = 4.611$, $p = .032$). Diagnosis of migraines was associated with diagnosis of bulimia nervosa ($\chi^2(1, N = 153) = 6.167$, $p = .013$) and binge eating disorder ($\chi^2(1, N = 153) = 6.709$, $p = .010$). Diagnosis of migraines was not associated with diagnosis of anorexia nervosa.

Conclusion: Individuals with migraine were also more likely to be diagnosed with an eating disorder. More specifically, those diagnosed with migraines were more likely to be diagnosed with bulimia nervosa or binge eating disorder. Future research should look for overlapping pathophysiological mechanisms in migraine, mood and eating disorders.

PO318

Headache epidemiology and outcomes

Incidence of cluster headache in Bulgaria, ruse district

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Introduction: Scarce epidemiological data exist on cluster headache (CH) in Eastern Europe, including Bulgaria. Incidence of CH has been estimated in few reports worldwide.

Aim: To study the incidence of CH in Bulgaria, Ruse district, regarding differences in demographics, clinical characteristics, triggers, diagnostic delay and treatment response.

Methods: We performed an observational retrospective cross-sectional study by using the ICHD-II beta version. We collected the data for 10 years from medical records of all admitted patients to the ER and Neurology unit, presenting with severe head pain with sudden onset. We hypothesized that all patients having a sudden onset of excruciating pain go to the ER or are sent to perform an imaging study. The multiprofile hospital (where the study was held), serves the whole district (population of 247 000 people) and it is the only one with an imaging lab.

Results: We estimated the incidence of CH in Ruse district to be between 1 and 5 in 100 000 people. We found out 39 patients with CH for the studied 10 years. We focused on actual age of patients, age of onset, gender, clinical characteristics, comorbid conditions, family history, triggers, smoking, diagnosis delay, treatment response, and some specific female gender issues.

Conclusions: CH is rare in Bulgaria. Because of existing differences in presentation and therapy response in forms and genders, CH is diagnosed with a significant delay. Up-to-date epidemiological and clinical data are essential because CH can be treated successfully and new alternative neuromodulatory methods can be applied.

PO319

Headache epidemiology and outcomes

Analysis of headache management in referral neurology emergency center in north eastern Iran

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Background: Headache is one of most common complaints more frequent than common cold. Most of patients presenting with headache have benign headaches that need symptomatic therapies and management.

Aim: The aim of this study was to analyze the management of headache patients presenting to the neurology emergency room at a university teaching hospital (Ghaem hospital) in Mashhad in north eastern Iran.

Method: Retrospective analysis of all patients with headache was carried out during first three months of 2014.

Results: Patients were analyzed according to the diagnoses, diagnostic procedures and treatment. From total of 650 patients with headache migraine with or without aura, tension-type headache had 579 (89%) patients (women 69% and men 31%); secondary headache had 71 (11%) patients: 39(6%) stroke or intracranial hemorrhage, 16 (2.5%) primary tumor, 13 (2%) metastatic tumor, and 3 (0.5%) had an infectious disease

Six hundred and thirty (97%) patients underwent computerized tomography scan of the brain.

Corticosteroids (dexamethasone) and chlorpromazine were the most commonly prescribed medications followed by fluids, simple analgesics and antiemetics (e.g. Intravenous metoclopramide) whereas opioids (e.g. intravenous morphine) were prescribed to 10% of patients.

Conclusion: In conclusion, approximately ninety percent had primary headache. The majority of patients were treated with Dexamethasone and a minority with intravenous opioids. Better treatment for these patients should be provided by emergency headache centers, specialized outpatient clinics and with developing standard guidelines in each center.

Keywords: Emergency Medicine Department, Dexamethasone, Headache

PO321

Headache epidemiology and outcomes

Study of headache after the great east Japan earthquake in iwate coast area (1)report of 2012

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Aim: To investigate prevalence of headache and headache-related factors after the Great East Japan Earthquake. **Methods:** We conducted medical inquiries concerning headaches in 2012 among municipalities with the greatest earthquake-related damage in Iwate Prefecture including Yamada Town, Rikuzentakata City and Heita District of Kamaishi City. Of 5958 individuals who responded to the survey we compared gender and age between the group with headache and without headache before and 1 year after the earthquake. One year after the earthquake we investigated mental factors (stress, nervousness, fatigability, sleep disorder, and K6score), past history, BMI, post-traumatic stress disorder (PTSD)–related factors caused by the earthquake, home-related factors (experience living in shelters or temporary housing residences), and interpersonal relationships.

Results: Headache prevalence was 22.6% before the earthquake and 25.4% one year later. Younger age and being female were associated with headaches at both time points. Factors related to having a headache were: having mental factors; not habitually consuming alcohol or smoking; not having comorbid metabolic syndrome, hypertension, diabetes, or gout; having PTSD-related factors caused by the earthquake; switching or losing jobs; having home-related factors; and not feeling mutual dependencies nor confidence with neighbors.

Conclusion: The survey revealed that the individuals who have headaches were relatively younger and had a greater number of females. It was suggested that mental factors such as stress, nervousness, fatigability, and sleep disorder, PTSD-related to the earthquake, home environment, and limited interpersonal relations may affect headache onset.

PO322

Headache epidemiology and outcomes

Study of headache after the great east Japan earthquake in iwate coast area (2)comparison between migraine group and non-migraine group

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Aim: To investigate characteristics between migraine group and non-migraine group after the Great East Japan Earthquake.

Method: We conducted medical inquiries concerning headaches in 2012 to investigate headache-related factors among municipalities with the greatest earthquake-related damage in Iwate Prefecture including Yamada Town, Rikuzentakata City, and Heita District of Kamaishi City. Of 5958 individuals who responded to the survey, 1506 indicated that they had headaches at the time of the survey. We investigated these 1506 individuals to compare mental factors (stress, nervousness, fatigability, sleep disorder, and K6 score), past history, BMI, post-traumatic stress disorder (PTSD)–related factors caused by the earthquake, home-related factors (experience living in shelters or temporary housing residences) and compared differences between two groups.

Results: Of 1506, there were 129 migraineurs (8.5%). Subjects in migraine group were younger and high frequency of women, high frequency of subjects with headache before the earthquake compared with non-migraine group. In migraine group compared to non-migraine group, subjects with early morning awakening and hypertension were less, and who subjects with smoking habit were larger in number. There showed weak association with PTSD by the earthquake and no relationship with home-related factors.

Conclusion: The survey revealed that the subjects in migraine group were younger and had a greater number of females. There were no difference in mental factor except nervousness. In non-migraine group, there were preferably higher relationship with PTSD by the earthquake and home-related factors.

PO323

Headache epidemiology and outcomes

Neuralgias of trigeminal terminal branches. Unfairly forgotten by III Edition of international classification of headache disorders?

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Background: International Classification of Headache Disorders, III Edition (ICHD-III) has not included neuralgias of peripheral branches of trigeminal nerve (nasociliary,supraorbital or other terminal branch).

Aim: To analyze incidence and characteristics of these disorders in a prospective headache registry.

Material Y Métodos: We evaluated consecutive patients with these diagnosis (codes 13.5, 13.6 and 13.7 in ICHD-II) attended in an outpatient headache office during a six-year period (January 2008 – January 2014). We collected demographic and clinical data.

Resultados: 43 patients (27 females,16 males) out of 3500 attended during the inclusion period (1.2%),and 237 (18.1%) with cranial neuralgias. Age at onset 45.5 ± 16.4 years (16–86). Most frequently diagnosed neuralgias were supraorbital (23 cases, 53.5%) and auriculotemporal (11, 25.6%). Latency between onset and diagnosis of 29.5 ± 32.4 months (1–140). In 35 patients (81.3%) background pain rated as 5.6 ± 1.3 (2–8) on verbal analogical scale (VAS) and in 22 (51.2%) exacerbations rated as 7.9 ± 1.3 (5–10) on VAS. Tenderness over the affected nerve in all cases. We offered a nerve blockade to all patients; in 26 (60.5%) at least one blockade was performed with complete relief lasting from 2 weeks to 6 months. In 22 (51.2%) at least one preventive therapy had been previously prescribed with partial or no effect.

Conclusion: Neuralgias of trigeminal terminal branches are not uncommon in a headache unit. Diagnostic delay observed in our series indicates a need for increasing their

understanding. So, in our opinion, these entities should be included in final version of ICHD-III.

PO324

Headache epidemiology and outcomes

Visual sensitivity in migraine: development and validation of the visual sensitivity questionnaire

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Background: Up to 60% of migraineurs report abnormal interictal visual sensitivity to patterns, light, or both. A well-validated questionnaire to quantify visual sensitivity is lacking.

Aim: To develop a Visual Sensitivity Questionnaire (VSQ) and to assess its internal consistency, test-retest reproducibility, and external validity.

Methods: We developed a 9-item questionnaire (5-point Likert scale) to assess interictal sensitivity to light and patterns. The questions were based on information from the literature, interviews with migraineurs, and migraine forums on the internet. Internal consistency for the VSQ was tested with Cronbach's α and item-total correlations. Test-retest reproducibility was assessed with intra-class correlation coefficient (ICC) (two weeks to one year later). For external validation the sum score of the VSQ was correlated with the pattern glare test (general illusion index) and the light sensitivity test (light discomfort threshold), using spearman's rho.

Results: A total of 171 migraineurs and 99 healthy controls completed the VSQ. Internal consistency assessed with Cronbach's α was 0.87, item-total correlations ranged between 0.46 and 0.72. Test-retest reproducibility ($n = 90$) assessed with ICC was 0.94. There was a significant correlation between VSQ sum-score and general illusion index ($n = 131$, r_s:0.443, $p < 0.01$) and VSQ sum-score and light discomfort threshold ($n = 49$, r_s:−0.396, $p < 0.01$).

Conclusions: The newly developed VSQ has an excellent internal consistency and reproducibility, and a good external validity. We demonstrated its ability to assess light and pattern sensitivity in migraineurs. The Visual Sensitivity Questionnaire is easy to use and allows future research on light and pattern sensitivity in larger populations.

PO325

Headache epidemiology and outcomes

Evaluation of thunderclap headache & its etiologies among kurdish patients (in tohid hospital of sanandaj-west part of Iran)

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Background: Headache is one of the most common causes for referring patients to clinics and most of the people have experienced severe and suddenly headache (Thunderclap) at least once in their lifetime.

Aim: This study aimed to investigate the common etiologies of thunderclap headache and associated symptoms in Kurdish patients in Sanandaj (West part of Iran).

Methods: This descriptive study was evaluated all patients with suspected thunderclap headache during 2013–2014 admitted to Tohid Hospital in Sanandaj. Data from the patients' files using descriptive statistics were used to describe the data.

Results: We performed this cross-sectional study during October 2013–Septemper 2014(within 1 year). The sampling method was census (statics) of all patients (about 119 patients) admitted to emergency ward of Tohid hospital during this period with severe and sudden (thunderclap) headache.

Conclusion: This study showed that the most common cause of thunderclap headache in emergency ward was subarachnoid hemorrhage (SAH) (25 percent), and then migraine & intracerebral bleeding (ICH), each one with 12/5 percent. Unlike many studies, is that migraine is the most common cause of thunderclap headache as generally but in emergency wards, SAH & ICH altogether are more common causes for this type of headache.

Keywords: Thunderclap Headache, Migrain, S.A.H, I.C.H

PO326

Headache epidemiology and outcomes

Migraine cure: a patients' perspective

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Migraine affects millions of people worldwide. Migraine prevention trials show in average 50% reduction in 50% of patients. Migraine cure is a topic of controversy among physicians, limited information on patients' perspective is available. We surveyed 1107 migraineurs, 835 (75%) women, 267 (25.0%) men, who fit IHS diagnostic criteria. Their access to medical care, preference for treatment and opinions on migraine cure definition were studied. All patients signed informed consent. Mean age was 34.8, 55.4% had episodic migraine, 44.6% chronic migraine (CM). Most patients (90.9%) looked for medical treatment, (61.5%) had some preventive treatment, 90.7% would like to be on prophylaxis, only 8.7% of those weren't, 73.1% consulted a neurologist. A significant number (46.1%) believed there is a cure for migraine. Patients marked what they considered good definitions for migraine cure, 38.6% said 'get faster recovery from an attack", 38.0% thought 'achieve 90% improvement in headache frequency", followed by 'have never more headaches in life" by 28.1%, 'have no more strong headaches" 25%, 'keep headache-free for one year" 15.1%, 'keep headache-free for one month"10% (15,2% in CM), and '50% reduction in headaches" by only 5.8%. A significant number of patients think there is migraine cure, but their definitions varies. Migraine cure can be achieved in clinical practice in the majority of patients according to their own definitions. The 50% headache reduction does not match patients' expectations. Discussing migraine cure with patients may be an opportunity for a more optimistic approach potentially improving headache outcomes.

PO327

Headache epidemiology and outcomes

Natural history of migraine with aura: preliminary results of eight months follow-up

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Background and objective: Migraine prevalence is estimated 11–13% for all continents and nearly 25% of migraineurs experience aura. There is conflicting evidence that reveals evolution and effects of aura on the course of disease. We aimed to investigate baseline features of MwA patients and to reveal course by time.

Method: Totally 229 subjects admitted to study. To establish transformation of variables statistically we used latent growth mixture model, and patients grouped with special variables. Three groups established to evaluate headache intensity by course. Headache intensity was significantly different for all groups and age, headache onset, duration and frequency were identical for all groups at baseline.

Results: Group-3 (most severe headache group) showed best response to treatment by time. Most of the patients have $<$10 days/months headache at baseline. Baseline headache frequency did not predicted course for 8 months follow-up. We used two groups to evaluate headache duration course by time. At the shorter headache duration (meanly one day) group; course of duration did not change by time. At the longer baseline headache duration (2–3 days) group; duration shortened for 4–6 months, but this well-being was not sustainable and at 8 months duration was same with baseline.

Conclusion: Phenotypic features of MwA and their course by time could help us to form treatment strategies and to forecast prognosis of disease. These preliminary results of our study support importance of longitudinally studies to reveal course of disease.

PO328

Headache epidemiology and outcomes

Prevalence of cranial autonomic parasympathetic symptoms in chronic migraine: usefulness of a new scale

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Background: Cranial autonomic symptoms (CAS) seem to appear in around half of migraine patients.

Objective: Our aim was to analyse the prevalence and profile of CAS, mainly of cranial autonomic

parasympathetic symptoms (CAPS), in a series of patients with chronic migraine (CM) according the new criteria for autonomic symptoms in the current IHS Classification.

Patients and Methods: We prospectively recruited consecutive CM attending our headache clinic. Five CPAS were surveyed: lacrimation, conjunctival injection, eyelid edema, ear fullness and nasal congestion. They were graded as 0 (absent), 1 (present and mild) and 2 (present and conspicuous); therefore the score in this CAPS scale ranges from 0 to 10 points. As a cranial autonomic sympathetic symptom (CSAS), we also asked on the presence of ptosis.

Results: We interviewed 100 CM patients. Their mean age was 45 years (18–63 years); 93 were females. Eighteen had no CAPS, while 82 reported at least one CAPS. There were only 6 patients with scores higher than 5; the mean and median CAPS being 2.1 and 2, respectively. Prevalence of CAPS was lacrimation (48%) > eyelid edema (38%) > ear fullness (29%) > nasal congestion (19%). Ptosis was reported by 42.

Conclusion: These results, by using for the first time an easy quantitative scale, confirm that (mild) CAPS are not the exception but the rule in CM patients. The score in this CAPS scale could be of help as a further endpoint in clinical trials or to be correlated with potential biomarkers of parasympathetic activation in primary headaches.

PO329

Headache epidemiology and outcomes

Headache in sickle cell disease

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Background: thereis a paucity of information on the characteristics of headaches in individualswith sickle cell disease (SCD). Identification of the type of headache symptomsexperienced is important for optimizing their medical management.

Aim: toprovide preliminary data on the characteristics of headaches in patients withSCD.

Method: SCDpatients attending the Lagos University Teaching Hospital (LUTH), and who hadexperienced at least one headache episode in the past one year, were studiedusing a detailed headache questionnaire based on the InternationalClassification of Headache Disorders (ICHD-2) criteria.

Results: therewere 92 patients; 39 (42.4%) male and 53 (57.6%) female. The age range was 13to 44 years; mean, 24.8 ± 6.7 years.

Frequent headaches were common,with 61.5% of males and 67.9% of females reporting one or more headacheepisodes per week.

Headache was bilateral in52.2%, non-throbbing in 57.6% and of mild to moderate intensity in 80.4%.

Headache was accompanied byphonophobia in 46.7%, photophobia in 19.6%, nausea and/or vomiting in 5.4%, andaggravated by routine physical activity in 56.5%.

Three (3.2%) patients hadheadache that fulfilled the ICHD-2 criteria for migraine while 63 (68.5%) had headachethat fulfilled the criteria for tension-type headache.

A family history of headachewas present in 18.5%.

Only 7.6% sought medicalattention for their headache. Majority (85.9%) took over-the-counter (OTC)simple analgesics for headache relief.

Conclusion: TTH was the commonest primary headache disorder in SCD patients attending LUTH

Headache was frequent but ofmild to moderate intensity and relieved with simple analgesics.

PO330

Headache epidemiology and outcomes

Headache, depression, anxiety and quality of life: associations in the eurolight project

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Introduction: Several studies have found associations between psychiatric and headache disorders, and both types of disorder impair quality of life (QoL). The Eurolight dataset has population-based evidence collected from 6,624 people.

Methods: Using bivariate analysis, estimating odds ratios (ORs) [with 95% CIs], we analyzed these data for associations between migraine, tension-type headache (TTH) or medication-overuse headache (MOH) on the one hand and depression or anxiety on the other. Headache disorders were diagnosed by questionnaire and algorithmically, applying modified ICHD-II criteria; anxiety and depression were diagnosed by HADS. Analyses were performed in males and females separately.

Results: MOH was most strongly associated with both psychiatric disorders: for depression, ORs (*vs* no headache) were 5.6 [2.3–13.8] in males, 5.9 [3.1–11.2] in females; for anxiety they were 9.3 [4.4–19.5] and 7.1 [4.5–11.2] respectively. Migraine was also significantly associated with both psychiatric disorders: for depression, ORs were 2.2 [1.4–3.5] and 1.9 [1.1–3.1]; for anxiety 4.1 [2.8–6.2) and 2.4 [1.8–3.5]. TTH showed associations only with anxiety: ORs 2.5 [1.7–3.7] for males, 1.5 [1.0–2.2] for females. In the population with headache, there were strong but somewhat complex associations between psychiatric comorbidity and poor (*vs* very good) QoL (in particular, OR 44.1 [12.4–57.1] for females with depression).

Conclusion: In this large cross-sectional study we confirmed the associations between headache and psychiatric disorders in both genders. MOH stood above migraine, while TTH showed comorbidity only with anxiety, significant only in males. Psychiatric comorbidity probably compounds the negative effect of headache disorders on QoL; this would not be surprising.

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Headache epidemiology and outcomes

Outcome of a headache center, integrating western-eastern medicine in Asia

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Purpose: To organize better headache service delivery, Japanese Headache Society proposed a system of regional headache center associated with a network of headache specialists and primary care physicians. Eleven regional headache centers were accredited by the board. The purpose of this study is to evaluate the role and the outcome of our headache center in the past 2 years.

Methods: We started Saitama International Headache Center collaborating with Saitama Medical University and a regional headache care network. Our team was 4 board-certified neurologists, nurses, psychologists, physical therapists and Eastern-medicine specialists (Acupuncture and Yoga). Specialized headache care based on ICHD and EBM was performed and the role of Eastern-medicine was evaluated.

Results: After we started headache center, patients increased to a total of 3,500 per year (3.5 times more than previous headache clinic as a part of neurology). The ratio of referred patients increased from 12% to 45%. In patients with migraine ($n = 2024$) headache frequency (days/month) reduced by 49% from 8.6 to 4.3 days/month ($p < 0.01$). When Eastern-medicine was added in 320 patients, significant satisfaction was reported by 59% of patients which significantly exceeded clinical improvement rate.

Conclusion: Better headache service may vary in different regions of the world. Present analysis provides support for the role of regional headache center in Japan. In addition to improving clinical outcome, "Headache Center Strategy" significantly increased doctor attendance, patient's referral and public awareness on headache medicine.

PO332

Headache epidemiology and outcomes

Not otherwise specified headache in the emergency department: how to handle the problem

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Background: "Not otherwise specified" (NOS) headache is a frequent diagnosis in Emergency Department (ED) (15.7%–46%), not specifically treated, and rarely referred to the Headache Centre.

Aim: To evaluate the efficacy of a dedicated neurologic Acute Headache Centre (AHC) in diagnosing and treating patients with ED diagnosis of NOS-headache.

Methods: A four-year prospective analysis of all consecutive patients accessing to the ED because of non-traumatic headache, discharged with a ED diagnosis of NOS-headache, and referred to the AHC was performed. Causes of presentation, diagnostic tests, consulting visits, therapies, AHC diagnoses (ICHD-II criteria), MIDAS scores, were analyzed using SPSS 21.0.

Results: Out of 3168 patients totally admitted in ED for headache, 285 patients (73.7% F; 26.3% M; mean age 42 ± 16 years) were enrolled. Severity of pain was the most frequent cause of presentation to the ED (28.8%). Ninety-seven patients (34%) underwent a cerebral CT. Neurologic visits were required in 48.8% of patients. The most administered ED therapy were NSAIDs (29.9%), triptans only 0.8%. Only 1.7% of patients started a prophylactic treatment in ED. AHC diagnoses were primary headache (76.1%), secondary headache (15.4%), and not classified headache (8.5%). Migraineurs were the majority of cases (60%). In the AHC, the most used attack treatment were triptans (49.3%), and 49.4% of patients initiated prophylaxis. Disability was elevated ($MIDAS = 48 \pm 41$), and reduced after AHC therapy ($MIDAS = 25 \pm 21$; $p = 0.03$).

Conclusions: A dedicated AHC is effective in classifying, specifically treating, and reducing disability of NOS-ED headache, and in identifying secondary forms not recognized and not properly treated in ED.

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Headache epidemiology and outcomes

Migraine and eustachian tube dysfunction: comorbidity or risk factor for chronification?

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Background: Migraine is a prevalent and disabling neurological condition. Some comorbidities were already established as risk factors for its chronification.

Aim: We hypothesize that Eustachian tube dysfunction (ETD) could be a risk factor for migraine chronification.

Method: We carried out a cross-sectional study in a headache clinic between 2011–2014, during which 103 migrainous patients were included. During regular clinical interviews, some of them spontaneously addressed tinnitus, hearing loss and popping sounds in the ears, which varied with pressure.

We performed a clinical screening with an ETD questionnaire (ETDQ-7) and tympanometry, and compared these results with a sex- and age-matched control group (CG) (65 non-migrainous subjects without otorhinolaryngological history).

Results: Statistically significant differences in clinical ETD were observed between migrainous patients and CG ($OR = 14{,}197$ [3,270–61,643]), and between chronic (CM) and episodic migraine ($OR = 3{,}493$ [1,416–8,617]), with Chi-square values of 19,343 ($p < 0{,}001$) and 7,748 ($p < 0{,}01$) respectively.

Although the prevalence of ETD among the general population is 0,9%, in our study it reaches 3,07% (CG) and 31,06% (migraine groups). This discrepancy could not be due to ETDQ-7, because its authors proved a 100% sensitivity and specificity.

Conclusion: These results support a probable correlation between clinical ETD and migraine in general, and between clinical ETD and CM, although these correlations do not reach statistical significance in tympanometric results. Thus we suggest increasing the sample size.

ETD could be a risk factor for migraine chronification, associated with those already known. The fisiopathological mechanism could be that snoring and sleep apnea favour the appearance of ETD.

PO334

Headache epidemiology and outcomes

Stress and medication-overuse headache: results from a population-based representative survey

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Background: Stressful events or fluctuating stress levels can trigger headache. Increasing stress is associated with increasing headache days. People with less coping resources tend to use more analgesics for headache. High stress is related to smoking, physical inactivity, and obesity which have also been linked to headache and pain medication overuse.

Aim: to examine the prevalence of high stress among individuals with medication-overuse headache (MOH) and to examine whether associations between MOH and healthy lifestyle behaviours is modified by stress.

Method: Questionnaires were sent to 129,150 adults. Those with headache $\geq$15 days per month for 3 months were classified as having chronic headache (CH) then further described as having MOH or CH without medication overuse. Stress was measured using the Perceived Stress Scale (10 questions). Respondents were grouped into stress score quintiles; the highest quintile designated as having the highest stress levels. Associations between headache and stress were analysed by logistic regression.

Results: 68,518 people responded to the questionnaire. By definition, the proportion of respondents in the highest stress quintile was about 20% of the entire sample. However, among those with MOH, 57.7% (95% CI: 54.3–61.2%) were in the highest stress quintile. CH with and without medication overuse had strong graded associations with stress, even after adjusting for sociodemographic factors and comorbidities. High stress plus smoking, low physical activity, and obesity had synergistic effects in MOH but not clearly for those who had CH without medication overuse.

Conclusion: Stress reduction is highly relevant in MOH management.

PO335

Headache epidemiology and outcomes

Step scheme with therapeutic local analgesia (TLA), security acupuncture, complementary integrative medicine to the actual fight of headaches, migraine as well as drug-induced long-term headaches

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Headaches count to the most frequent discomfort in Germany: 66.7 percent of the women (24 millions) and 53.2 percent of the men (18.5 millions) have once a year headaches. Medical costs lie with 462 million euros / years. The indirect costs amount to 2,3 billion euros. Fifteen million people suffer from migraine. The period in which drug-induced long-term head pain develops lies for painkillers free on sale with 4,7 years, for Triptane with 1,7 years. 2% (1,64 millions) of the Germans have drug-induced long-term headaches.

The anaesthetic-saving therapeutic Lokalanalgesie free of side effect, poor in pain without ct. screening and X-ray screening to the treatment of therapy resistant pains, opioidtoleranter pains, tumor pains, with security acupuncture, physiotherapy, psychotherapy, phytotherapy, TENS, Moxibution, bleeding according to the Trang step scheme can relieve headaches, migraine as well as drug-induced long-term headaches or heal.

With prick technology as well as professional-shaped infiltration blockades are carried out by ganglion Stellatum spinal nerves HWS2-HWS7/Th1, Plexus cervicalis HWS2-HWS7 / TH1, Plexus brachialis, Nervus accessorius as well as local infiltration of the hardened cervical muscles up to the shoulder middle.

The acute headaches can reduce blockade of ganglion pterygopalatinum above Os zygomaticum, Nervus vagus with Emesis as well as prick technology to the blockade of the Nervus supraorbitalis medialis et lateralis, Nervus suprathrochlearis and Nervus infrathrochlearis to TRANG as

well as local infiltration of the painful places up to the BWS and acupuncture immediately to 0%.

With this combination therapy all patients get a better quality of life.

PO336

Headache epidemiology and outcomes

Spreading depolarization-modulating drugs and delayed cerebral ischemia in patients with subarachnoid hemorrhage

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Background: Delayed cerebral ischemia (DCI)occurs in approximately one third of patients with aneurysmal subarachnoidhemorrhage (aSAH). A proposed underlying mechanism for DCI is spreadingdepolarization (SD), which also occurs during a migraine aura. In a small series of aSAH patients, a temporal and spatialcorrelation between SDs and the occurrence of DCI was found.

Aim: Investigated the influence of use ofSD-modulating drugs on the occurrence of DCI.

Method: aSAH patients with data on use ofhome medication prior to hospital admission, occurrence of DCI, and clinicaloutcome were included. Home medication was classified as SD-inhibiting,SD-facilitating, or SD-neutral based on an comprehensive literature review. Weperformed Cox and Poisson regression analysis and calculated hazard ratios (HR)and risk ratios (RR) for the influence of SD-modulating drugs on our primaryoutcome measure DCI and secondary outcome measure poor clinical outcome(modified Rankin Scale $\geq$3) three months after aSAH. We adjusted for age, genderand clinical condition on admission (aHR/aRR).

Results: DCI occurred in 343 (29%)of 1194 patients. Patients using SD-inhibiting home medication had an aHR forDCI of 0.66 (95%CI 0.42–1.06) and an aRR for poor outcome of 1.13 (95%CI0.90–1.41). Patients using SD-facilitating drugs had an aHR for DCI of 1.24(95%CI 0.83–1.87) and an aRR for poor outcome of 1.19 (95%CI 0.95–1.50).

Conclusion: Use of SD-inhibiting drugs tended toreduce DCI, which could be an indication for a possible link between SD, Migraineand DCI. However, this did not result in a better clinical outcome.

PO337

Headache epidemiology and outcomes

The effect of embolization of pulmonary arteriovenous malformations on migraine among patients with hereditary hemorrhagic telangiectasia

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Backgrounds: Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant disorder characterized by epistaxis, telangiectasia, and arteriovenous malformations. About 30% of HHT patients have pulmonary arteriovenous malformations (PAVMs), and high prevalence of migraine with aura. Embolization of PAVMs is to reported to ameliorate migraine among HHT patients.

Aim: To determind the prevalence of migraine in the HHT patients with PAVMs and evaluate the effect of embolization of PAVMs on severity of their migraine.

Method: All the 50 HHT patients, diagnosed by the Curaçao criteria (only definite cases included), who were hospitalized to our medical center from January 2009 to December 2014 were included. Headaches were diagnosed according to the international classification of headache disorders, 3rd edition. Medical records and telephone interviews were used.

Results: The average age on admission was 33.0(from 6 to 77). There were 22 females. 40 out of the 50 patients had PAVMs. 13 patients with PAVMs had headache (migraine with aura, MA, 7, migraine without aura, MoA, 1, probable MoA, 1, others 4). Their prevalence of migraine was 20.0%, high as compared to 8.4% in the general population of Japan. After embolization of PAVMs, among 2 migraine patients (1 MA, 1 MoA), headache disappeared. 5 migraine patients (4 MA, 1 probable MoA) had less severe headache attacks. 2 MA patients had no effects on their headaches.

Conclusions: The HHT patients with PAVMs had high prevalence of migraine. Embolization of PAVMs decreased severity of migraine among HHT patients.

PO338

Headache epidemiology and outcomes

Quality of diagnosis and management of headache in the general population

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Background: Three successive editions of the international classification of headache disorders and multiple guideline papers on headache care have described evidence based diagnosis and treatment of headache disorders. It remains unknown, however, to which extent this has improved the diagnosis and management of headache in the general population. It was the aim of our study.

Methods: We studied 1042 students (719 females, 323 males, mean age 20.6, age range 17–40),1075 workers (146 females, 929 males, mean age 40.4, age range 21–67) and 1007 blood donors (484 females, 523 males, mean age 34.1, age range 18–64). We conducted a semi-structured, validated, face-to-face professional interview. Data on prevalence and associated factors have previously been published. A section of the interview focused on previous diagnosis and treatment, the topic of this presentation.

Results: Only 496 of 2110 participants (23%) with headache had consulted because of headache. Students consulted more frequently (35%), workers and blood donors less often (13% and 14% comparatively). 53% consulted neurologists and 41% GPs. Only 12% of the patients with ICHD-3beta diagnosis of migraine and 11% with ICHD-3beta diagnosis of tension-type headache had been correctly diagnosed. Triptans were used by only 6% of migraine patients. 3.7% of the patients (2.9% with TTH and 0.8% with migraine) used analgesics $\geq$15 times per month. Only 0.4% of migraine patients and no TTH patients had received prophylactic treatment.

Conclusion: Despite existing guidelines about diagnosis and treatment both remain poor in the general population. Dissemination of existing knowledge should have higher priority in the future.

PO339

Headache epidemiology and outcomes

The clinical features of 226 migrainous vertigo patients in neurological department

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Objective: To evaluate the common symptoms of both clinic and hospitalized migrainous vertigo patients in Neurological Department of general hospitals, so that clinical misdiagnosis and missed diagnosis could be reduced.

Methods: Clinical data of 226 migrainous vertigo patients was collected. Clinical features were evaluated according to medical history, clinical symptoms and signs, as well as results of diagnostic examinations.

Results: The order of occurrence of vertigo or migraine was not fixed. Types of vertigo and duration time were various and some patients have no headache symptom during the whole course.

Conclusions: There are various manifestations, some regularities as well as complex mechanisms of migrainous vertigo. Differential diagnosis with similar diseases should be paid more attention to.

PO340

Headache epidemiology and outcomes

Prevalance of primary headaches in shift workers in chemical industry: a population study

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Today is known that exposure to occupational risk factors have a relationship with the onset of headache. However is more important the exposure to non-causal factors that facilitate the emergence of an attack in patients already suffering from primary headaches.

Health surveillance and medical history questionnaires targeted 95 workers (91 males). The work in night shifts

interest 50 workers (52.6%), while 45 workers (47.4%) worked in the round of daily work. The shift system was kind of anterograde and always performed on three shifts.

The headache with higher prevalence was represented by migraine without aura (51.5%), followed by episodic tension headache (42.5%) and migraine with aura (6%). Considering male population, the data show a significant association between the prevalence of primary headache and outreach work night shift. Although numerically appreciable, the difference in prevalence did not reach statistical significance considering the four female employees.

Considering only male workers, the prevalence of primary headache was 42% in shift workers and 22% among others. The study shows a significant association between the conduct of work in night shift and the onset of headache. Is documented in the literature the negative effect that night work has on the state of mental and physical well-being. A possible negative effect of work at night as headache trigger seizures in people with acute primary headache has already been. To date are few studies that have shown an association between shift work and headache. The results of our work strengthens the hypothesis that the two events may be associated.

PO341

Headache epidemiology and outcomes

Migraine and mortality in elderly

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Introduction: Migraine is affecting 12% of the general population. Previous study have shown that migraine, in particular migraine with aura, was associated with an increased risk for vascular events, but the association between migraine and mortality rest uncertained.

Objective: To test the association between migraine and mortality from all causes in elderly individuals

Methods: Prospective cohort study among 1173 participant of the Epidemiology of Vascular Aging Study who provided information about migraine status. Participants were classified as having non-migraine headache, migraine or no-headache. A logistic regression was used to evaluate the relationship between migraine and total mortality.

Results: Among the 1173 participants, between 63 and 75 years old at baseline, 164 reported migraine and 66 reported non-migraine headache. Only 27 participants of the migraine described migraine aura, not allowing to calculate risk estimates for mortality. We found an association between migraine headache and total mortality suggestion a reduced risk (brut odds ratio 0.53; 95% confidence interval 0.31 – 0.88) when compared with participants that reported no headache history, but, after adjusting for age, sex and multi variables, the association became not significant statistically (adjusted odds ratio = 0.65; 95% confidence interval 0.38 – 1.11). Non migraine headache was also not associated with total mortality (brut odds ratio = 0.95; 95% confidence interval 0.49–1.11; adjusted odds ratio = 0.91; 95% confidence interval 0.47 – 1.77).

Conclusion: Migraine or non-migraine headache was not associated with an increase of total mortality in elderly people. Selective survival may explain discrepancies compared to other findings.

PO342

Headache epidemiology and outcomes

The use of symptomatic drugs in self medication headache patients: one year follow-up

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Background: Medication-overuse headache (MOH) is a worldwide health problem with a prevalence of 1%–2%. Italy is the first European country for OTC consumption with related problems of self-medication and risk of MOH.

Aim: monitoring the consumption of symptomatic drugs for headache and preventing drugs abuse/dependence.

Materials and methods: 276 patients using self-medication symptomatic drugs for headache were recruited in 32 pharmacies in the Pavia Health District. A telephonic interview was carried out in 199 patients; 179 entered the study at baseline (T0) and 87 (13 M and 74 F, mean age 45.0 ± 11.5 years) were followed-up at 12 months (T12).

Results: At T12 the number of days/month with headache vs T0 were significantly reduced (3.1 ± 3.4 vs 9.6 ± 8.6; $p = 0.0001$), the same goes for attacks/month (respectively: 2.04 ± 1.8 vs 7.6 ± 8.1, $p = 0.0001$), and the duration of the single attack (hours) (respectively 8.5 ± 15.1 vs 38.2 ± 34.8, $p = 0.0001$). Besides, the mean headache intensity/attack was found to be slightly reduced at T12 vs T3 (4.4 ± 2.8 vs 4.6 ± 2.5, $p = 0.04$). An increase in quality of life was found on MIDAS scores at T12 vs T0 (16.7 ± 35.1 vs 22.7 ± 27.7, $p = 0.005$) and in the quality of treatment received (HURT)(5.5 ± 5.4 vs 9.8 ± 5.5, $p = 0.0001$). The clinical data of patients drop out (n = 92) were compared to those who ended the study.

Conclusions: The change from self medication regime to medical care may reduce the headache days/month, the intensity of attacks and ameliorate the quality of life in patients with headache.

Acknowledgments: RG from the Italian Ministry of Health (2013–2014) to IRCCS C. Mondino.

PO343

Headache epidemiology and outcomes

Headaches in mitochondrial disorders

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Background: Headaches are a well-known feature of Mitochondrial Disorders (MCDs). However, no systematic epidemiological data are available in large populations of patients.

Aim: We aimed to describe the prevalence and the headache's characteristics of a large group of patients with mitochondrial encephalomyopathies.

Methods: We studied all consecutive patients referred to our Neuromuscular Unit, during a 6-months period. 93 patients (ages 15 to 78 years, 31 males) with a typical phenotype of MCDs, underwent a structured diagnostic headache interview, using an operational diagnostic tool following the IHS criteria. If they met the criteria for primary headache, were included in'Headache Group' (HEAD+). The other patients were collected in 'No-HeadacheGroup' (HEAD−). Clinical, neuroradiological, and neurophysiological data were compared between groups. Mann-Whitney U-test was used to analyze numeric variables. Fisher exact test was used to analyze nominal variables. Binary logisticregression analysis was performed to identify risk factors of headache.

Results: Headaches were reported in 35.48% of patients. Migraine was the most common headache. HEAD+ showed younger age (HEAD+ = 45.5 ± 17.2 years; HEAD− = 54.5 ± 14.8 years; U-test = 7.393; p = 0.007), increased prevalence of epilepsy(p = 0.0103), myoclonus (p = 0.0309), stroke (p = 0.0290), EEG focal slow abnormalities (p = 0.0359), EEG epileptic focal abnormalities (p = 0.0425), and decreased prevalence of muscle weakness (p < 0.0001), and EEG normal pattern (p = 0.0136). Multivariate analysis showed that HEAD+ was significantly associated with absence of Muscle Weakness (CI = 1.007–14.894; p = 0.049) and EEG abnormalities (CI = 1.347–78.085; p = 0.025).

Conclusions: Migraine have higher prevalence in MCDs compared to population-based data. Our findings are consisted with the widely hypothesized role of mitochondria in migraine pathophysiology.

PO344

Headache epidemiology and outcomes

The comprehensive headache-related quality of life questionnaire: status report

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Background: The Comprehensive Headache-related Quality of life Questionnaire (CHQQ) is a new

headache-specific QOL questionnaire, developed at the Department of Neurology. Semmelweis University (Budpaest, Hungary), and validated in migraine and tension type headache. In order to facilitate further research, based on the idea of communion, gratuity, and reciprocity in research, the questionnaire is publicly accessible through a purpose-built website. A number of scientific projects using the CHQQ are underway.

Aim: To present the ongoing work and future directions of study concerning the CHQQ.

Methods: Description of ongoing research based on our research database.

Results: Validation studies of CHQQ's Hungarian version in other headache types (chronic migrane, cluster headache and medication overuse headache) are underway. The linguistic validation of the questionnaire has been completed in English and Farsi, and its Serbian version is currently being validated. The linguistic validation processes in German and Italian are expected to be completed by December 2015. Validation studies of the English and Farsi versions are conducted in migraineurs. Investigator-initiated clinical studies using the questionnaire are conducted in 3 Hungarian centres and also in India (Bangalore and New Delhi), Iran, and the United States. The questionnaire's homepage, http://headache-questionnaire.com hosts an online English version that will also be utilized for accumulating data about the QOL of persons who have not yet consulted medical services because of their headaches.

Conclusion: The ongoing studies in various languages and headache types will hopefully contribute to establish the role of the CHQQ in assessing the burden of different headache types.

PO345

Headache epidemiology and outcomes

Integrated care model for headache patients: a piloting assessment

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Background: Innovative 'Integrated Care" programs are among the most effective and efficient way for deploying healthcare services delivery. By a 'patient-centered" vision, they allow to effectively integrate the diverse levels of care (primary, secondary and tertiary) supported by evidence based clinical protocols. On this basis, they guarantee continuity of care and efficient use of health care resources.

Aim: Experimentally assess the effectiveness and efficiency of advanced 'cephalalgic integrated care" program, characterized by evidence based and well planned clinical workflows and supported by technological platform providing informative and decision making services.

Method: We define and develop the architectural organization of the proposed integrated care program, based on collaborative patient-centered 'nested close-loop approaches". The program 'integrates" the healthcare operators (GP, secondary specialist, tertiary specialist) and the relevant clinical processess through the several healthcare settings, guaranteeing adherence to the most recent clinical guidelines. In order to evaluate the performance of the care program, we design an experimental study based on 10 Primary Care, 5 Secondary Care and 1 Tertiary Care providers and enrolling 50 patients. Baseline visit and follow up observation have been carried out for each patient. Relevant appropriateness and outcomes indicators have been selected and collected during the study

Results: The study is developing from six months and the preliminary results confirm the effectiveness and efficiency of the proposed integrated care program.

Conclusions: The integrated care management of headache patients allows more effective and efficient healthcare service delivery, improving the related outcomes and making the best use of available healthcare resources.

PO346

Headache epidemiology and outcomes

Epilepsy and headache: a cross-sectional study in 125 patients with temporal lobe epilepsy

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Objective: To establish relations between epilepsy and headache and evaluate patters of treatment in these patients.

Background: Headache is a common comorbidity in epilepsy, but remains poorly understood and overlooked.

Methods: Cross-sectional study of 125 patients with temporal lobe epilepsy. Patients (after assign the informed consent) were divided in three groups according with the age of epilepsy onset. We studied their headache and epilepsy, and its characteristics.

Results: The mean age of patients were 44.5 years old (SD $\pm$ 11.3) and 73 of them (58.4%) were women. Seizures were classified as focal without impairment of consciousness in 31 patients (20%), generalized in 92 (59.4%), and focal with impairment of consciousness in 32 (20.6%). One hundred and two (81.6%) of our patients with epilepsy had headache. Migraine was present in 55 (44%) of them. Headache was more common in patients that started epilepsy at younger ages (<50 y $=$ 38,3%; >50 y $=$ 7,8%). Seventy-eight patients (77.5%) use analgesics for pain treatment and 24 (30.5%) of them used it in a self-medicated form.

Conclusion: In our cohort, headache occurs in two-thirds of patients with temporal lobe epilepsy. Headache was more frequent when epilepsy started at younger ages. The treatment of headache in epilepsy has been overlooked and self-medication is common in these patients.

Perspectives: Patients with epilepsy and headache use analgesics in a self-medicated manner, which is inappropriate. Neurologists should be aware that headache is a very common comorbidity in epilepsy, is frequently overlooked and have been inappropriately treated in these patients.

PO347

Headache epidemiology and outcomes

Cutaneous allodynia and migraine: systematic review

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Background: During migraine attacks, activation and sensitization of the trigeminovascular system is implicated in the development of a lowering of the pain threshold to ordinarily non-painful stimuli known as allodynia. Studies have demonstrated that approximately two thirds of migraneurs experience cutaneous allodynia.

Aim: Our primary aim was to systematically review studies of migraine and allodynia focusing on the frequency and impact of allodynia in migraine. The secondary aims were to review types of allodynia, to describe various methods of assessment and to identify variables of significant association with allodynia in migraineurs. We also consider diagnostic and treatment implications.

Method: PubMed and EMBASE were searched to identify potentially eligible studies. Eligible original studies were published prior to November 2014, used ICHD diagnostic criteria for migraine, and assessed patients for the presence of allodynia. Candidate studies were reviewed and eligible studies were abstracted.

Results: Two population-based and fifteen clinic-based primary studies were eligible to assess the relative frequency of allodynia in migraine which ranged from 42.7% to 91%. Thirty-six articles were eligible for analysis of features associated with allodynia in migraine. The relative frequency of allodynia is higher in women than men and

Table 1. Relative frequency of allodynia in persons with migraine in clinic-based studies by method of assessment and migraine type

Authors Sample size Source of sample Subject gender and age	Method of assessment	Relative frequency of allodynia Ictal or interictal assessment Migraine subtype: episodic, chronic or both, with or without aura	Additional data if reported: Time at which allodynia assessed Allodynic diagnostic criteria Allodynia subdomain analysis Severity scoring criteria and analysis
Misra et al. N = 448 Headache center; Median age: 32 years; 77.6% female	QST for mechanical static, mechanical dynamic, thermal allodynia	Ictal episodic or chronic migraine: 320 (71.4%) with ≥ 1 type of allodynia (20 patients with chronic migraine, remaining were episodic)	Allodynia assessed at headache onset. Static mechanical allodynia was more common (90.6%) than dynamic mechanical (89.1%) or thermal (17). In most of the patients, allodynia was elicited by multiple stimuli
Guven et al. N = 186; Neurology clinic; older than 18 years; 167 females	ASC 12-item questionnaire	Ictal episodic migraine with or without aura: 114 (61.3%)	Allodynia assessed during headache. Allodynia severity was mild in 62 (54.4 %), moderate in 36 (31.6 %), severe in 16 (14 %). No relation of allodynic subtypes with demographic/clinical characteristics of migraine except for menstrual migraine
Lovati et al. N = 221; Headache Center; Mean age 37 – 41 ± 13, 192 females	8-item questionnaire	Ictal episodic migraine with or without aura or chronic migraine: 117 (52.9%)	Allodynia assessed during migraine attack
Ashkenazi et al. N = 151; Headache clinic; 125 females 34.4 ± 1.0 years of age	16-item questionnaire	Ictal episodic migraine with or without aura: 116 (77%)	Patients assessed during and between migraines, with 139 (92%) and 132 (87%) citing ≥1 symptoms of skin hypersensitivity, respectively. A patient was classified as allodynic if citing any one-questionnaire item. Of 116 allodynics, 62 with heat allodynia, 41 with cold allodynia. Most common was ponytail (82), least common was shaving (3)
Mathew et al. N = 295; Headache clinic; 259 Females; Mean age was 39 ± 3.2	12-item questionnaire	Ictal episodic migraine with or without aura: 157 (53.3%)	Patients reported ≥1 allodynic symptoms during or within 48 hours of attack. Pillow allodynia reported by approximately 15%. Combing, brushing, and hair-washing allodynia in 30%
Kao, et al.	17-item symptom	Ictal episodic or chronic	Total allodynia score from 0 - 17. Severity: no

N = 434; Headache clinic; 349 females; Mean age 40.7 ± 13.4 years	checklist	migraine with or without aura: 210 (48.4%)	allodynia (0–2), mild allodynia (3–5) and moderate - severe allodynia (≥ 6). Average number of allodynic symptoms was 4.3 +/- 3.1
D'Agostino, et al N = 410; Headache center; 80% Females; Mean age: 36 ± 10.6 years	Italian version of ASC questionnaire	Ictal chronic or episodic migraine with or without aura: 258 (63%)	No CA (scores 0–2), mild (3–5), moderate (6–8), and severe (>9). 39.7% with mild allodynia, 25% moderate, 35.3% severe. Allodynia in 26% of males, 74% of females, severe in 38.7% females, 1% of males
Lovati et al. N = 175; Headache center; 37 Females; Mean age: 29.9 ± 10.2 years	8-item questionnaire	Ictal episodic or chronic migraine with or without aura: 97 (55.4%)	Allodynia defined as scalp sensitivity or discomfort during HA + positive response to ≥ 1 of 7 assessed activities. Episodic migraineurs: CA in 60 (48.4%), Chronic migraine: CA in 37 (72.5%)
Burstein et al. N = 31; Pain clinic; Mean age: 36.2 ± 1.9 (17-55); No gender data	Thermal and static mechanical QST	Ictal episodic migraine: 19 (61.2%)	Assessed on 3 occasions: migraine free, one and four hours after HA onset. Pain thresholds decreased from 45.6°C to 40.1°C for heat, increased from 12.7 to 20.7°C for cold; decreased from 112.6 to 29.8gm for mechanical skin stimulation
Ashkenazi, et al. N = 89; Headache clinic; 75 Females; mean age 44.5 ± 11.9 years	Brush allodynia with 10 x 10 cm gauze pad	Ictal exacerbation of chronic migraine: 16 (45.7%) ictal baseline chronic migraine: 22 (40.7%); Overall: 38 (42.7%)	16 (45.7%) were allodynic during migraine exacerbation, 22 (40.7%) were allodynia during baseline headache. BA was most common in the V1 area, followed by the C2–C3 dermatome, and was least common at the C8 dermatome
Ashkenazi et al. N = 38; Headache clinic; 79% Female, Median age: 25.5 years	Dynamic mechanical brush allodynia	Ictal episodic migraine with or without aura: 30 (79%) Interictal episodic migraine with or without aura: 18 (39%)	Assessed both between and during untreated attack. Total allodynia score ranged from 0 to 600 (max of 100 at each skin site x 6 sites)
De Tommaso, et al. N = 333; Pain center; 280 Females: Mean age: 41.34 ± 14.4	Italian version of Ashkenazi 16-item questionnaire	Ictal chronic migraine with or without aura: 303 (91%)	Patients assessed during migraine attack. Allodynia defined as presence of ≥ 1 symptom reported in the questionnaire, for ≥ 50% of HA episodes.
Bevilaqua-Grossi, et al. N = 15; Headache clinic; 73.3% female;	ASC-12 questionnaire	Ictal or interictal episodic migraine per ASC: 7 (46.6%)	Criteria for allodynia: score ≥ 3 at any time over one month. ASC estimated presence of allodynia over 3-month period, QST was used to obtain an immediate

(continued)

Table 1. Continued.

mean age 45.9 years			and objective measure of allodynia. By ASC: mild allodynia in 2 (13%), 0 with moderate, 5 (33%) with severe. ASC subdomains: total: 4.8, thermal: 2, mechanical static: 1.7, mechanical dynamic: 1.1
Guy et al. N = 67; Headache clinic; 58 women; mean age: 40 ± 2 years (16 - 69)	Guy et al. 19-item questionnaire	Ictal episodic migraine: 49 (73%)	Allodynia criteria: positive response to ≥ 1 of 19 items in questionnaire during or after migraine attack. Cephalic CA mechanical in 92%, isolated in 52%, associated with thermal in 40%. Extracephalic allodynia thermal in 75%, alone in 42% and with mechanical in 33%. Pure mechanical in 25% of extracephalic allodynics.
Tietjen et al. N = 1413; 11 Headache centers; 1240 (88%) female; mean age: 42 ± 0.5 years	Tietjen et al. 6-item questionnaire	Ictal episodic or chronic migraine with or without aura: 857 (60.7%)	Allodynia criteria: ≥ 1 of 6 items during migraine. Most common: pillow CA, combing hair. 10% of population reported ≥ 4 allodynic symptoms
Jakubowski et al; N = 89; Headache center; 79 women; mean age: 37.9 ± 1.1 years|	Jakubowski et al. 12-item questionnaire and QST (cold and heat thermal, mechanical)	Ictal episodic migraine with or without aura by QST: 66 (74%) Ictal episodic migraine with or without aura per questionnaire: 84.8% of the 66 patients classified as allodynic by QST	Assessed during and between attacks. Allodynia criteria: sensitivity 1 of 3 QST modalities or ≥ 1 positive response to 1 of 12 items in questionnaire. QST: 52 (79%) with mechanical allodynia, 50 (76%) with cold allodynia, 43 (65%) with heat allodynia. 29 (44%) with allodynia to all 3 modalities, 10 (15%) with cold + heat allodynia, 7 (11%) with mechanical + cold allodynia, 4 (6%) with mechanical + heat, 12 (18%) with mechanical alone, 4 (6%) with cold alone
Lipton et al. n = 11,388; AMPP population project; 75.6% female; Age range 18 to > 75 years	ASC 12-item questionnaire (See LIST-1)	Prevalence of ictal episodic or chronic migraine with or without aura: 7197 (63.2%)	Allodynia mild in 25.1%, moderate in 17.1%, severe in 20.4%. Thermal allodynia correlated 0.76 with static mechanical allodynia, 0.71 with dynamic mechanical allodynia. Static mechanical + dynamic mechanical allodynia highly correlated with interfactor correlation of 0.69.
Louter et al. n = 2331; LUMINA population study; 85.5% female; mean age: 42.8 ± 11.4 years	12-item questionnaire adapted from ASC questionnaire	Prevalence of baseline ictal episodic migraine with or without aura: 1624 (70%)	Allodynia severity and subdomain analysis data not reported

increases with age, with aura and with headache days per month. Allodynia is also more common in persons with comorbid pain conditions, depression, anxiety and fatigue (see Table 1).

Conclusion: The wide variation in the observed coexistence of allodynia and migraine results from differences in study samples, migraine features, methods of assessing allodynia and comorbidities.

PO349

Headache and gender

The observation of women with migraines during pregnancy in the republic of bashkortostan

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Introduction: According to clinical studies 60–70% women suffering from migraines during pregnancy notice significant improvement of their state especially in the first and the second trimester that is seemingly associated with estrogen synthesis stabilization. (Sances G. Granella F. et al 2003).

Aim: To study the course of migraine attacks in women during pregnancy.

Method: The research group consisted of 114 women suffering from migraines in past medical history before pregnancy. The diagnosis was defined in accordance with ICHD 3rd edition (beta version) criteria. The women were observed during pregnancy. The study included: headache diary, estimation of headache intensity according to visual analogue scale (VAS), anxiety and depression levels.

Result:

Table 1. Dynamics of headache intensity and migraine attacks number during pregnancy

Pregnancy trimesters	Pain Intensity (VAS, mm)	Migraine attacks number (days)
I	85,29 ± 1,74	8,80 ± 0,66
II	62,22 ± 1,72	5,4 ± 0,60
III	57,57 ± 2,53	3,20 ± 0,40

Conclusion: As a result of our research the following dynamics has been detected: in women suffering from migraines without aura who followed all the recommendations (regime, avoidance of food containing tyramine) the total remission of migraine attacks has been observed.

In women with frequent migraine attacks in the past medical history the number of attacks during pregnancy decreased twofold but the attacks were followed by aura.

Disclosure: The predictors of migraine intensity decrease and total remission of migraine attacks are background disease characteristics (migraine type and attacks frequency) hormonal status (placental secretion of progesterone and estradiol for pregnancy safety), carrying out of recommendations for migraine attacks prevention.

PO350

Headache and gender

Long-term contraception with the progestin desogestrel 75μg reduces migraine frequency and use of acute medication: A diary –based study

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Background: Premenopausal migraines frequently are associated with fluctuations of estrogen levels. Both, migraine and combined hormonal contraceptives (CHC) increase the risk of vascular events. Therefore progestagen-only contraceptives (POC) are a safer alternative.

Aim: To study the long-term effect of the POC desogestrel 75 μg on migraine frequency, intensity, use of acute medication and quality of life.

Methods: Patients charts were screened for women with migraine, who had decided to use desogestrel for contraception. Charts were included, if routinly conducted headache diaries were complete for a treatment period of 180 days Baseline data (90 days) were compared with first and second treatment period (90 days each). Quality of life was evaluated using MIDAS questionnaires.

Results: Days with migraine (5.8 vs.3.6), with any kind of headache (9.4 vs. 6.6), days with severe headache (5.4 vs.2.4) and use of triptans (12.3 vs.7.8) were significantly reduced after 180 days. MIDAS score and grade improved significantly.

Conclusion: Contraception with desogestrel 75 μg resulted in a significantly improved quality of life and a reduction of migraine days over the observation period of 180 days. As also triptan use declined this progestin might lower the risk of developing medication overuse headache in a subgroup of women. For counselling reasons it is of importance, that although the major reduction in migraine frequency occurs during the initial 90 days there is further bettering possible in the long-term.

PO351

Headache and gender

Headache and gender- a study in our hospital

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Headache is one of the most common of medical complaints but inspite of this it still remains largely underdiagnosed, undertreated and also neglected in medical teaching. Migraine is the most common cause for disabling headaches that are seen in practice. The World Health Organisation (WHO) in their recent report identified migraine to be among the world's top 20 causes of disability, with an impact that extends beyond the suffering individual.

Migraine is estimated to account for 2.0% years of life lost due to a disability in women of all ages. In both sexes, migraine is responsible for 1.4% of total years of life lost due to a disability. These results are anticipated to have long-reaching impact on individual sufferers, their caregivers, family and on society itself.

Aim: To study the cases of headache and compare

Material and Methods: A total number of 100 patients who presented to the medical OPD with complaint of headache. Careful and appropriate history was taken in all the patients. The study wsa conducted over a period of 1 year from september 2013 to august 2014.

Result: The cumulative lifetime incidence of headache in the population studied is 67 percent for females and 33 percent for males.

Conclusion: Headache is seen more commonly among females and it produces maximum disability during peak productive years of ones lifetime.

PO352

Headache and gender

Headache in transgendered patients

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The transgender population is estimated to be 0.025–0.1% of the population worldwide. There are two ways that patients can approach this transition; if done early providers can halt the onset of puberty and the use of hormone therapy can alter a patient's sexual course, or after puberty hormone suppression and supplementation can be implemented. This has created a new patient population with unique medical and psychological comorbidities.

Previous studies have implicated sex hormone components leading to an increased incidence of migraines in females once they reach puberty and throughout their adulthood to menopause. Research suggests that a significant drop in estrogen levels within the normal female menstrual cycle is a trigger for migraines. Because of this hormonal component, it is a reasonable to think that patients undergoing gender change will encounter changes in their headache incidence, frequency and severity.

Starting with a systematic review of the literature, I have found that there is currently little published data addressing the question of headache incidence in this patient population. Given the presence of artificially steady hormone levels, as opposed to the fluctuating hormone levels seen in the non-transgender population, this is an interesting question worth investigating. This could lead to more data to help unravel the underlying mechanisms that drive the headache brain.

I will be collecting data on headache frequency and severity in the transgender population, before and after hormone replacement via a survey to determine classification of headache (using ICHD3 beta criteria), incidence and severity.

PO353

Headache and gender

Association of MDR1 C3435T polymorphism and antiepileptic prophylactic therapy response in Turkish migraine patients (preliminary results)

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Background: Antiepileptic drugs are commonly used in migraine prophylaxis. Genetic polymorphisms in multidrug resistance 1 (MDR1) gene are involved in development of drug resistance. In the literature, there is no published study evaluating the association between drug resistance in prophylaxis of migraine patients and MDR1 C3435T (rs1045642) polymorphism. In this study, presence of MDR1 C3435T polymorphism, in anti-epileptic therapy (AET) migraine patients and its possible effect on therapy resistance were investigated.

Methods: A total of 166 (F: 151, M: 15) migraine patients from our outpatient headache clinic were enrolled in this study. MDR1 C3435T polymorphism was analyzed on the DNA samples obtained from peripheral blood of the patients by Polymerase Chain Reaction (PCR) – Restriction Endonuclease Fragment Length Polymorphism (RFLP) method and data was confirmed with automatic sequence analysis device (Beckman Coulter). Association between responses to prophylaxis with anti-epileptic drug and MDR1 C3435T polymorphism was evaluated.

Results: 82 subjects were on AET, 63 of those were resistant to the AET, 19 responded to the AET. In the treatment resistant group (n: 63), %79.4(n:50) showed MDR1 C3435T polymorphism, 15 out of 19 subjects showed MDR1 C3435T polymorphism in the treatment responded group. MDR1 C3435T polymorphism showed significant difference between treatment resistant and responded groups ($p = 0{,}034$).

Conclusion: Possibility of development of AET resistance in patients with MDR1 C3435T polymorphism should be considered AET for patient menagement.

PO354

Headache and gender

Influence of the natural estrous cycle on the threshold for potassium induced cortical spreading depression in mice

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Background: Ovarian hormones are believed to be important modulators of cortical spreading depression (CSD), which is known to be implicated in a variety of disease conditions, including migraine aura. In this study, we explored the change of serum concentration of ovarian hormones and the threshold for CSD occurrence in response to potassium stimulation during the natural estrous cycle in C57BL/6J mice.

Methods: The natural estrous cycle of mice was divided into estrus and diestrus stages by checking the smear specimens of vaginal cytology. The induction of CSD was monitored by recording DC potentials at an electrode. A small open cranial window was installed near the electrode, and initially, 0.025 M potassium was applied to it. Gradually potassium concentration was increased by 0.025 M until CSD was induced. The serum concentrations of estradiol and progesterone were also measured by liquid chromatography.

Results: The minimal potassium concentrations to evoke CSD were 0.26 ± 0.05 M in estrus ($n = 7$) and 0.11 ± 0.05 M in diestrus ($n = 7$). In diestrus, the minimal potassium concentration required to evoke CSD was significantly lower compared to estrus ($P < 0.05$). In diestrus, the serum concentration of estradiol was 3.18 ± 1.51 pg/mL($n = 11$), and was significantly higher than the estrus (0.97 ± 1.45 pg/mL; $n = 10$).

Conclusion: These data indicated that estradiol may play an important role with regard to the susceptibility to the development of CSD in the estrous cycle in female mice.

PO355

Headache and gender

Sexual function and distress in premenopausal women with medication overuse headache (MOH)

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Background: women treated for primary headaches in a tertiary university center have shown a high rate of sexual symptoms and distress.

Aim: to investigate sexual function and distress in premenopausal women with medication-overuse headache (MOH).

Method: we recruited 149 still menstruating patients who had signed an informed consent to fill-in the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale-Revised (FSDS-R), as part of the psychometric assessment during hospitalization. Data on pharmacological history (symptomatic and preventive drugs) were also collected.

Results: mean age of our study sample was 39.4 ± 8.2 years (range 20–55) and median BMI was 22.2 (95% CI: 21.5–23.1) kg/m^2. The majority had at least 13 years of education (79.9%) and were in a stable relationship (72.5%). No sexual activity (last 6 months) was reported by 16.1% of women (13 with stable partner, 11 with no or casual partner). Female sexual dysfunction [FSD (FSFI cut-off score $\leq$26.55)] was diagnosed in 89 women (59.7%), whereas sexual distress (FSDS-R cut-off $\geq$15) was documented in 71 women (48.3%). Hypoactive sexual desire disorder (HSDD) was found in 51 women (34.7%). Median n° of symptomatic drugs per month was 34 (95% CI: 30–40), whereas 57.1% of MOH patients were on preventive drugs (30.2% one; 26.9% two). Interestingly, sexual distress was significantly higher ($p < .03$) in those using more than one preventive drug.

Conclusion: these preliminary results suggest that sexual function should be routinely assessed in specialised

headache centres because FSD and distress, including HSDD, may be part of the headache-related disability.

PO356

Headache and gender

Sex matters: estrogen and testosterone levels in male migraineurs at baseline and preceding an attack

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Background: Migraine prevalence is three times higher in women during the fertile lifespan and their attack frequency is correlated with fluctuations in the levels of reproductive hormones. Data on reproductive hormones in male migraine patients, however, are lacking.

Aim: We assessed whether baseline levels ofandrogen and estrogen are different in male migraineurs and whether changes in these levels may precede attacks.

Methods: Levels of free testosterone (T_f), estrogen (E2) and the T_f/E2 ratio were assessed in 18 male migraine patients and 22 age and BMI matched headache-free male controls. Blood samples were collected four times daily on one baseline day in both groups. Additionally, migraineurs were measured longitudinally daily, until the onset of the next migraine attack. Baseline levels were compared with (repeated measurement) ANCOVAs. Longitudinal data in migraineurs were analysed by a Generalized Estimated Equations model.

Results: T_f/E2 ratio at baseline was lower in migraineurs vs. controls: 3.92 ± 0.37 vs. 4.98 ± 0.34; $p = 0.04$, with higher E2 levels (96.78 ± 6.06 vs. 69.11 ± 5.57; $p = 0.002$). Baseline T_f levels did not differ (357.47 ± 21.41 vs. 332.55 ± 18.73; $p = 0.40$). In migraine patients, during the premonitory phase, T_f/E2 ratio ($p < 0.001$) was higher compared to baseline due to higher T_f levels ($p = 0.003$).

Conclusion: Male migraineurs have higher baseline estrogen levels compared to non-headache controls, possibly reflecting higher migraine susceptibility. Levels of free testosterone increase during the premonitory phase of a migraine attack, which might reflect activation of nociceptive pathways.

PO357

Headache and gender

Migraine and women: how much influence on the choices of motherhood?

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Introduction: Migraine is one of the most frequent diseases recognized as a cause of disability, with a relevant influence on the quality of life, particularly in women.

Aim and method: Our study proposes to evaluate whether migraine affects reproductive choices and motherhood. We interviewed 399 women affected by migraine without (93,5%) and with (6,5%) aura, aged 17–79 years, using a semi-structured questionnaire. We collected data about attacks intensity and frequency, fertility, pregnancies, abortion/miscarriage, children number, influence on decisions about pregnancy and perceived ability in motherhood.

Results and conclusion: Among the 399 women interviewed, 94(23,6%) were post-menopausal while 305(76,4%) had their menses; 155 (38,8%) were nulliparous while 244(61,2%) had had at least one pregnancy; 224(56,1%) were mothers while 175 (43,9%) did not have children.223 (55,9%) had less than 5 attacks/month, 130 (32,6%) had 5 to 14 attacks/month, 46 (11,5%) had 15 or more attacks/month. Pain intensity was low (NRS 1 to 4) in 18 (4,5%), moderate (NRS 5 to 7) in 108(27,1%), high (NRS 8 to 10) in 273 (68,4%). Among the 399 women we interviewed, of those who wanted another child (184; 46,1%), 60/184 (32,6%) considered their headache a problem for a pregnancy. Among patients who did not want (further) pregnancies (215; 53,9%), 20/215(9,3%) listed headache among the causes for this choice. 227 on 399 women (56,9%) reputed headache an impediment to their being mothers. Our results seem to show a negative influence of migraine on decision of facing pregnancy and self-perception as mothers, maybe contributing in perceived disability.

PO358

Headache and gender

Sinusitis and headache

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Materials and Methods: Examinations were conducted on 87 patients ageing (27–57) years old with chronic headaches from the Hospital in Poznan (Poland) Department of Neurology and Ophthalmology during. The patients were diagnosed with migraine headaches and divided into 2 groups.

Group 1 consisted of 57 patients, whereas group 2 of 30 patients. In both patients groups, head MR, OCT of fundus and V, T examinations were performed. In 12 patients, no association with infection was diagnosed, while detailed diagnostics towards glaucoma was started.

Results: In 18 patients from group 1 head MR indicated mucosal thickening of the maxillary sinus and ethmoid bone, whereas in 21 patients of the frontal sinus. In the nasopharyngeal swabs of the microbiological examination S.pneumoniae was detected in 11 patients of group 1, M. catarrhalis in 13 patients, S. aureus in 9 patients and K.oxytoca in 7 patients. In 4 patients from group 1, glaucoma was diagnosed.

In the control group (group 2), in the nasopharyngeal swabs, S aureus was detected in 8 patients, S pneumonia in 4 patients, M.cattrahalis in 3 patients and K.oxytoca in 2 patients. In only one patient, glaucoma was diagnosed.

Conclusions: 1. Patients with chronic headaches in sinus area should have routinely performed microbiological examinations, aiming for rapid diagnosis and proper treatment introduction.

2. Patients complaining of specific headache expect from primary care physician medical referral to a specialist neurologist or ophthalmologist to perform expensive and detailed examinations, while in certain cases diagnostic method sufficient for determining diseases is a routine microbiological examination.

PO359

Headache and gender

Pain perception in women with menstrually related migraine

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Background: Migraine incidence and severity vary throughout the stages of fertility and the menstrual cycle, along with estrogen levels. We recently reported that menstrual cyclicity of estrogen levels and dermal blood flow responses are disturbed in women with menstrually related migraine (MRM) (Neurology 2015;84:1–7).

Aim: This case-control study aims to explore differences in pain perception of women with MRM after estrogen levels drop in the menstrual cycle (day 1–2; follicular phase) as compared to a period with high estrogen levels (day 19–21; luteal phase).

Method: Premenopausal women with MRM ($n = 14$) and their healthy controls ($n = 10$) were asked to grade pain at cycle day 1–2 and day 19–21, for different concentrations (6.0 mg/mL, 0.06 mg/mL) of capsaicin and electrical stimulation on the forehead skin, a dermatome innervated by the trigeminal nerve. Electrical stimulation of the skin in the neck, application of high pressures with sphygmomanometer and venipuncture were reference measurements of peripheral pain. Pain in postmenopausal women ($n = 15$) was measured twice with an interval of 7–10 days.

Results: Reported pain for the trigeminal dermatome, but not peripheral pain, was lower at day 1–2 than at day 19–21 of the cycle in healthy women. This was significantly different ($p < 0.05$) in women with MRM, who reported equal pain in either phase. Postmenopausal women also reported similar pain levels during both visits.

Conclusion: Our observation of decreased cyclicity of trigeminal pain perception in women with MRM is in accordance with our earlier findings of reduced variation in trigeminovascular activity throughout the menstrual cycle.

PO360

Headache disorders in children and adolescents

Prevalence and disability of headache among Norwegian adolescents: a general population-based study

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Background: Headache is common in adolescents and affects schoolwork and relations with friends and family. In most previous epidemiological surveys, only the most bothersome headache has been documented. The aim was to determine headache prevalences taking into account not only the most bothersome headache, also to compare characteristics of the most bothersome and less bothersome headaches, and to investigate headache-related disability.

Methods: A cross-sectional school-based study was conducted, where 493 representative adolescents aged 12–18 years were recruited by stratified cluster sampling and interviewed. Headache diagnosis was made according to the new classification system of the International Headache Society (ICHD-3 Beta), and the Pediatric Migraine Disability Assessment (PedMIDAS) was used to evaluate disability.

Results: The one-year prevalence of any headache type, migraine, probable migraine and tension-type headache was 88%, 23%, 13% and 58%, respectively. The point prevalence of any headache was 38%. Nine percent of subjects fulfilled criteria for more than one headache diagnosis. The most bothersome headache had a significantly longer duration ($p < 0.001$) and higher intensity ($p < 0.001$) than the less bothersome headache, but similar frequency ($p = 0.86$). Adolescents with headaches lost up to nine days of activity each year, implicating headache as a major health issue.

Conclusions:. Headaches are very common and disabling among adolescents. The full extent of this health problem is better appreciated if inquiry is not limited to the most bothersome subtypes.

Keywords: Adolescents, Headache, Migraine, Tension-type headache, Prevalence, PedMIDAS.

PO361

Headache disorders in children and adolescents

Pediatric migraine – epidemiology & characteristic features of aura

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Objective: To assess the characteristics and epidemiological features of pediatric migraine with aura.

Background: About 80% of children and adolescents have headache. The prevalence of migraine in children is about 8%. Approximately 15–30% of children and adolescents with migraine report of aura.

Methods*:* Children presenting with headache to three pediatric neurologic clinics in Haifa (Bnai Zion Hospital, Carmel Hospital and Meuhedet Medical Services) in the last 5 years were assessed. Inclusion criteria included: migraine headache in children 5–18 years of age. Data regarding: age, gender, headache classification, aura, and family history were assessed.

Results: Of the 262 children (140 female) who had migraines, 26.2% experienced aura. A greater percentage of female children experienced aura as compared to male children (32.6% vs. 18.9%, $p < 0.01$). Children who experienced aura were older than patients who did not experience aura (13.1 vs.11.5 years, $p < 0.001$). Females had a higher rate (66.7%) of visual aura compare to males (33.3%) ($p < 0.04$). There was an association between family history of migraine and children experiencing aura ($p < 0.02$) with the odds of experiencing aura 2.79 times greater in children who had a family history of migraine than children who had no family history.

Conclusions: Migraine with aura is as common in children as it is in adults. Aura is more common in females and older children. Children with family history of migraine are more likely to have aura, which should raise a question about the diagnosis of migraine without aura in every child without a family history of migraine.

PO362

Headache disorders in children and adolescents

Acute cerebellitis in children: a many faced disease

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Background: Acute cerebellitis is a rare inflammatory condition often characterized by signs and symptoms related to acute elevation of intracranial pressure such as severe headache, vomiting and decline of consciousness. Additionally, there may be cerebellar signs such as acute truncal ataxia and dysmetria. It may have a benign, self-limiting course; however, it may present as a fulminant disease resulting in severe cerebellar damage or even sudden death.

Aim: To present our experience with acute cerebellitis in children. The clinical, diagnostic, therapeutic features and outcome of this entity will be described.

Method: We retrospectively reviewed the clinical, laboratory and radiological data of patients diagnosed with acute cerebellitis at the Schneider Children's Medical Center of Israel between January 2000 until November 2014.

Results: Nine children aged 3.5 to 12.5 years were diagnosed with acute cerebellitis at our medical center. Bilateral diffuse hemispheric involvement was the most common imaging presentation. Two patients manifested tonsillar herniation and hydrocephalus. Mycoplasma pneumoniae infection was the pathogen in four children and West Nile virus in one. Four patients had a good prognosis with full recovery, while the other five suffered from residual neurological complications.

Conclusion: Acute cerebellitis is a rare pediatric disorder. It may present with acute severe headache and may evolve to a life-threatening condition. Early recognition and treatment are necessary to change this course to a benign outcome. MRI is the modality of choice to demonstrate cerebellar pathology (which may not be detected in CT) and to differentiate this entity from a neoplasm.

PO363

Headache disorders in children and adolescents

Clinical features of headache in children and adolescents at an outpatient pain clinic in Japan

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Background: Children and adolescents frequently experience headaches. Although they usually visit pediatric clinics, some of them visit pain clinics. However, there is little information about the clinical features and therapeutic efficacy of headache patients who visit pain clinics.

Objective: To investigate the clinical features of children and adolescents who visit an outpatient pain clinic for management of headaches as well as the efficacy of the treatments.

Methods: In this single hospital-based retrospective study, we enrolled patients aged $\leq$15 years, who had headache and visited our pain clinic between 2013 and 2014. We obtained information on clinical background, diagnosis, response rate and adverse effects of acute-phase therapy, and prognosis from their medical records.

Results: Twenty-two patients (M:F = 8:14; mean age, 12.1 $\pm$ 2.6 years) were enrolled. Twenty of the 22 patients (91%) were diagnosed as having migraine, including migraine without aura (13 patients; 59%), migraine with aura (7 patients; 32%), and secondary headache disorders (2 patients; 9%). Eighteen of the 22 patients (82%) had already received medical treatments at previous hospitals, although headache was not treated successfully. Acetaminophen was not effective for these patients. However, triptans such as rizatriptan and eletriptan were used for the treatment of the headache in 14 of 20 patients with migraine, and all patients were treated successfully. Triptans did not produce serious adverse effects. Patients did not prefer nasal sumatriptan because of its bitter taste.

Conclusions: More than 90% of children and adolescent patients with headache who visited a pain clinic had migraine. Triptans were effective and well-tolerated.

PO364

Headache disorders in children and adolescents

Venous discirculation and headache syndrome

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Research objective: Assessment of cerebral venous hemodynamics inchildren and teenagers having cranialgia with updating cause-effect relationsof venous discirculation.

According to the data ofUltra Sonic Testing (in C- and PW- modes) 109 patients (at the age from 2 to18) it was found that discirculation in thesystem of vertebral veins is linked with apparent extravasal effects onblood-stream in internal jugular vein (with vessel compression on the side ofvasoconstriction registration) ($r = +0.67$), spasms of posterior cerebral artery ($r = +0.63$), coiling of internal carotid andvertebral artery ($r = +0.20$ $+0.32$). In case of discirculation in the system of internal jugular vein, the changesmentioned are interrelated with extravasal compression on the level of internaljugular vein surrounding soft tissues or compression in the bone canal ($r = +0.76$),anterior cerebral artery spasms, hyperperfusion of vertebral and posteriorcerebral artery ($p < 0.05$). Intracranialvenous discirculation depends on the straightness of vertebral artery in thebone canal ($r = +0.33$), discirculation intensity on the level of vertebral vein (Vmaxright $r = +0.73$, $p > 0.05$).

Vasoconstriction inthe vein of Galen is accompanied by ipsilateral hypersthenia of vertebral, internalcarotid and middle cerebral artery (reflectory changes), and is alsointerrelated with flexures, sigmoid coiling of internal carotid artery.

The link of "headachesyndrome" with accelerated venous blood flow along the veins of Galen turnedout to be quite low ($r = +0,22$).

Conclusion: Main causes of children's vasoconstriction are eithercongenital pathology of cervical spine (with arcuation and tortuosity of bone canal),or "birth injuries with pseudo-luxation of cervical vertebrae".

PO365

Headache disorders in children and adolescents

Relationship between primary headache and functional gastrointestinal disorders assigned by questionnaire on pediatric gastrointestinal symptoms rome III version (QPGS-RIII) in Siberian adolescents: school-based screening study

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Many common complaints in adolescent medicine practice, such as recurrent headache and recurrent abdominal pain (RAP) have similar risk factors, accounting for emotional stress, anxiety and depression. Data regarding the association of these conditions are limited.

Methods: 511 urban (Krasnoyarsk, Siberia) adolescents aged 12–17 years were examined by previously tested questionnaire based on ICHD-II criteria with high diagnostic accuracy for migraine (sensitivity – 92 %, specificity – 93 %) and for clinical relevant tension-type headache (TTH, including the subtypes 'frequent episodic TTH, chronic TTH", sensitivity – 97 %, specificity – 93 %). Simultaneously, adolescents were tested with QPGS-RIII. Two-tailed exact Fisher was used, data are shown as %.

Results: Significant positive associations were detected between functional dyspepsia and both subtype of functional dyspepsia – TTH (<0.001), migraine (<0.001, Table 1); as well as between irritable bowel syndrome and migraine ($p = 0.001$). Slightly positive association was

Table 1. Association between recurrent headache and recurrent abdominal pain.

Headache	Functional Dyspepsia n = 8		Irritable Bowel Syndrome n = 35	Abdominal Migraine n = 13	Functional Abdominal Pain n = 16	Functional Abdominal Pain Syndrome n = 10
No headache (1) n = 445	0.7		5.8	2.0	2.9	1.8
TTH (2) n = 38	10.5		7.9	5.3	5.3	2.6
Migraine (3) n = 28	3.6		21.4	7.1	3.6	3.6
p	p1-2 < 0.001	p1-3 < 0.001	p1-3 = 0.001	p1-3 = 0.081	–	–

between abdominal migraine and headache migraine ($p = 0.081$).

Conclusion: Strong relationship between headache and functional gastrointestinal disorders can result from the effect of psychosomatic components. The high level of functional dyspepsia in headache adolescents may also results from analgesics overuse in "headachers" and/or iron deficiency due to Helicobacter pylori infection in adolescents with upper RAP.

PO366

Headache disorders in children and adolescents

Primary headache in urban Siberian adolescents: prevalence and psychopathological comorbidity with strengths and difficulties questionnaire (SDQ) assessment

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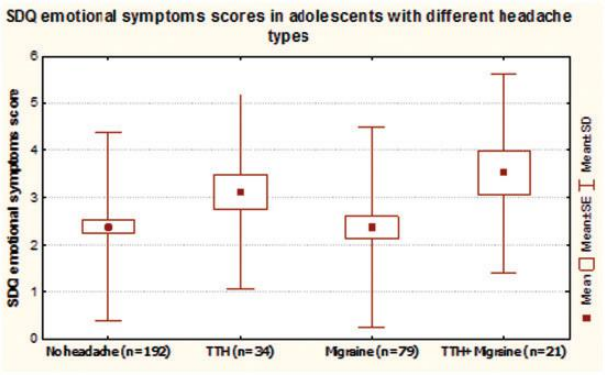
Data regarding the headache prevalence according to ICHD-II criteria and the SDQ assessment in varies types headache in Russian adolescents are limited.

Methods: 1012 urban Siberian (Krasnoyarsk, Russia) adolescents aged 12–18 years were examined by specially trained neurologist to diagnose the headache subtypes (12 month prevalence). Based on ICHD-II criteria, a classification of migraine (including the subtypes "with or without aura"), and tension-type headache (TTH, including the subtypes "infrequent episodic TTH, frequent episodic TTH, chronic TTH") were given. 326 adolescents were tested with self report version of SDQ questionnaires. Kruskal-Wallis test was used for differences assessment.

Results: According ICHD-II criteria one or more types of headache were diagnosed in 75.3 % adolescents: TTH in 43.8 % (infrequent episodic TTH – 36 %, frequent episodic TTH – 5.2 %, chronic TTH – 2.6 %), migraine in 13.5 % (without aura – 8.6%, with aura) – in 1.9 %. Mixed type of headache (in subjects fulfilling the diagnostic criteria for both probable migraine and probable TTH) was diagnosed in 16.1 %. A strong positive association was detected between frequent episodic and chronic TTH presence and SDQ emotional symptoms score ($p < 0.021$, Figure 1). No differences have been found in conduct problems, peer problem, and prosocial behaviour scores, as well as, SDQ total score.

Conclusion: Headache prevalence is high in Russian adolescents and its structure has no principal differences between previously reported worldwide data. Frequent episodic and chronic TTH is strongly associated with psychopathological comorbidity such as emotional problems.



PO367

Headache disorders in children and adolescents

Migraine in children. Abnormalities of brahiocefalic vessels

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Abnormalities of brahiocefalic vessels are one of the reasons of different diseases from functional disturbances to stroke. However there is a lack of information concerning children.

The main purpose of our work was to define value of abnormalities of brahiocefalic vessels in children with migraine.

Materials and methods: 45 children (24 migraine with aura, 21 – without aura) aged 5–17 years old have been examined. Blood flow in brahiocefalic vessels was recorded by Ultrasonic Transcranial Doppler and Color-Coded Duplex.

Results: We revealed structural abnormalities of brahiocefalic vessels in 62% of children: 50% – internal carotid arteries (ICA), vertebral arteries (VA) – 32%, combined abnormalities – 18%.

We have registered at 60% of children with S-shaped deformation of ICA and at 15% of children with kinking of ICA reduction of cerebral blood flow more than 18%. At 33% of children with hypoplasia of VA decrease of intracranial blood flow of VA more than 45% is revealed. Heavier symptoms of migraine (during aura – frequent syncope, expressed disartria, sensitivity violations) and the period between attacks (headache, vegetative violations, sleep disorders) are found in children with abnormalities of brahiocefalic vessels.

Conclusion: Disturbances of hemodynamic abnormalities of brahiocefalic vessels make significant influence on a functional condition of brain and clinical picture of migraine in children.

PO368

Headache disorders in children and adolescents

A child with recurrent attacks of ophthalmoplegic migraine

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Introduction: Ophthalmoplegic migraine(OM) is a poorly understood neurological syndrome characterized by recurrent headaches with paresis of the ocular cranial nerves. The third cranial nerve is most commonly affected;the fourth and sixth nerve less so. The etiology, pathophysiology, and definitive treatment of OM remain unclear.

Case: A 12-year-old girl was admitted to our hospital with a 2-day history of abrupt right diplopia and ophthalmoplegia associated with a sharp and throbbing headache in the right temporal area. Interestingly, the patient had experienced 2 similar attacks since her age of 5 years. In each episode, the attack lasted for about 2 weeks and diplopia and ophthalmoplegia unilaterally presented in her right eye. There was no family history of any similar diseases or migraines. On neurological examination, complete right third nerve palsy with pupillary sparing was noticed. Other systemic examinations and laboratory tests were normal. A brain MRI with contrast enhancement revealed remarkable focal thickening with intense enhancement was noted in the right third cranial nerve.

Conclusion: On the diagnosis of OM, severe headache and right eye ptosis and diplopia completely resolved after high dose steroid therapy. The findings in our case emphasize the difficulty of OM diagnosis, even with new IHS criteria, because patients rarely fulfill all of the relevant characteristics at the same time.

PO369

Headache disorders in children and adolescents

Influences of behaviral and psychiatric factors on treatment effects in the school-age children with migraine

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Purpose: School-aged children with severe migraine might need medication, and often accompanied by a psychiatric or behavioral problems. Thus, study for the effect of its problems on treatment of severe pediatric migraine is very important. Materials and Methods: among the 197 school-aged children who were diagnosed as migraine by ICHD-3b, seventy-two patients who need prophylactic therapy were enrolled from January 2012 to December 2013. Secondary headaches and headaches with ADHD or require psychiatric treatments were excluded. Before treatment, all patients were checked by Childhood behavioral checklist(CBCL), Children's Anxiety Scale(CAS) and Children's Depression Inventory(CDI) for screening of behavioral and psychological problems, and administered with topiramate(25–50 mg hs) as a prophylactic medication. They were followed-up at intervals of 2–4 weeks and grouped as good responder(GR) and poor responder (PR).

Results: A total of 72 patients was M:F;28:44, mean-age; 11.2 ± 2.7 years. GR(45 patients; 62.5%, M:F;18:27, age; 10.7 ± 2.5) and PR (27; 34.7%, M:F; 10:17, age; 12.0 ± 3.0) were no statistically different. Features of headache in GR(duration; about 6 mo, attack duration; 9 h, frequencies; 12/mo) and PR(duration; about 12 mo, attack duration; 4 h, frequencies; 16/mo) had no significant difference. T-scores of GR and PR group were statistically different in total behavior problems, internalizing problems, depression/anxiety, social immaturity, attention problems of CBCL($p < 0.01$), but not different in factors of depression or anxiety in CAS and CDI.

Conclusion: Because behavioral factors affect the treatment children with migraine, it is important to selection of drugs or management of behavioral problems.

PO370

Headache disorders in children and adolescents

Ictal and periictal headache in children with epilepsy – correlation with type of seizures and EEG-changes

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Introduction: Data from the literature show that 34–47 % patients with epilepsy suffer from periictal, mainly postictal headache. There are poor information about correlations between type of headache and children's age and sex, type of seizures, type of eeg changes, localization of headaches and differentiation if the headache is preictal, ictal or postictal in children.

The aim of the study was to evaluate the frequency of the preictal, ictal and postictal headaches in children with epilepsy and correlation between these symptoms with types of seizures and changes in eeg.

Material and methods: The prospective study conducted in the Department of Developmental Neurology in Medical University of Gdańsk, include 30 patients, 6–17 years old, with established epilepsy diagnosis and periictal headaches. The study group was divided into three subgroups according to the headache: preictal, ictal or postictal.

Results: In 76% children focal seizures, in 40% secondary generalized and in 16% primary generalized seizures were observed. 73% patients suffered from postictal headache, ictal headache occurred very rarely (7%). The mean intensity of the pain measured with the VAS scale was 6,5. We found the correlation between lateralization of headache and interictal changes in eeg in patients with focal seizures.

Conclusion: The frequency of periictal headaches correlates with type of seizures and type of changes in eeg.

PO371

Headache disorders in children and adolescents

Migraine with aura in children: a retrospective analysis

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Background: Migraine with aura is a recognized as a subtype ofmigraine and few studies are reported about migraine with aura in pediatricpopulation.

Aim: To analyze the clinical features of headache and auracharacteristics.

Method: We analyzed retrospectively charts of children-affected by headache referred to Headache Center of Bambino Gesù PediatricHospital between 2000 and 2011.

Results: 166 patients were included in the study. Headache frequency was sporadic in 43.5 % ofcases. Pain was frontal in 43.9% of cases. Headache duration was comprisedbetween 1–2 hours in 38.9% of patients. Aura was characterized by visual (86.6%), sensitive (12.7%) including aphasic disturbance, motor (0.7%) or acombination of them. Furthermore, aura was classified in preictal (67.3%), ictal (22.7%) or pre and ictal (10%) as regards headache onset. Aura durationresulted comprised between 5 to 10 minutes in a 32.7% of cases. We found that aless duration of aura (ranged from 5 to 10 minutes) correlated significantlywith a sporadic frequency of migraine with aura ($p < 0.05$); duration of aurawas also inversely correlated to throbbing pain of headache ($p < 0.001$) andwas shorter in younger children ($p < 0.001$). Visual aura was frequentlyassociated with photo- and phonophobia ($p < 0.05$). Visual aura with positivesymptoms (scintillating scotoma) was significantly correlated to a shorterduration of migraine attack.

Conclusion: Many features of migraine with aura reported inchildren show some peculiarities to be further investigated. Our study may beuseful to improve our current knowledge of migraine with aura in children.

PO372

Headache disorders in children and adolescents

Chronic primary headaches in children and adolescents referred to two third level headache centres

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Background: The prevalence of chronic migraine (CM) and chronictension-type headache (CTTH) increases with age, as it was especially shown inrecent years. As for pediatric age, some points, including the prevalence ofmedication overuse headache (MOH) in chronic headache children and thechronification rate in children with episodic primary headache, remain stillobscure.

Aim: The aim of the present study was to investigate theclinical characteristics of children with chronic primary headaches (CPH).

Method: We performed thispreliminary retrospective epidemiological study in 2012 and included 5000 charts of children referring to the Headache Centres of both Ospedale BambinoGesù and Insubria University Hospital.

Results: Among all 5000 childrenwith diagnosis of primary headache, referred to both Headache Centres, 270 patients (5.4%) received the diagnosis of CPH. This diagnosis was predominant in girls (66.4%). As for headachecharacteristics, 34.3% of CPH children were classified as CTTH, while 53.7% had a diagnosis of CM. Headache characteristics were undefined in the remaining 12% CPH children. New daily persistent headache (NDPH) and Medication Overuse Headache accounted for 16.29%and 5.6% of CPH, respectively. Among NDPH patients, most of them (80%) showed migraine characteristics of their headache.

Conclusion: Our results showed that CM is the most important cause of CPH in both children and adolescents. Interestingly, we confirm the highprevalence of NDPH patients in pediatric CPH, far higher than that reported in adult CPH (around 6%). On the contrary, as expected, the rate of MOH in our CPH population was low.

PO373

Headache disorders in children and adolescents

Juvenile migraine and allodynia: results of a retrospective study

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Background and aims: there are only two small sample studies investigating allodynia in the pediatrci population. Aims of this study was to evaluate frequency of allodynia during cephalalgic attacks in a juvenile population with primary headache and its associations with other symptoms of migraine.

Methods: we rewied all medical record of patients with primary headache consecutively seen in a two years period. Frequency of allodynia was evalueted, by means of a questionnaire, consisting of six questions (for example: Do you avoid touching your head when you have a migraine attack?).

Results: 230 children suffering for primary headache were seen during the study period. 202 children were affected by migraine, 28 (12.2 %) by other primary headaches. Migraineurs significantly more frequently complained of allodynia compared to other primary headaches (37% versus 0%). At multivariated analysis, allodynia was significantly associated with pain aggravated by physical activity (OR a 2.0, 95% CI 1.0, 3.8), phonophobia (ORa 2.3, 95% CI 1.0, 5.1), and nausea (ORa 1.9, 95% 1.0, 3.7).

Conclusion: Accord in to our data allodynia is common during pediatric migraine attacks. The associations between allodynia and physical activity, nausea and phonophobia are supported by studies on adult population and suggests specific physiopatological mechanisms.

PO374

Headache disorders in children and adolescents

Prevalence of tension type headache in children and adolescents with temporomandibular disorders heading for orthodontic treatment

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Background: Temporomandibular Disorders (TMDs) is a common term used to describe signs and symptoms in the trigeminal system. The complexity of the problem may cause confusion regarding etiology, diagnostics and treatment effectiveness. There is only sparse number of papers focusing on therelationship between TMDs and other afflictions including tension type headache (TTH) in children/adolescents.

Aim: The aim of the study is the analysis of the relationship between TTH and signs/symptoms ofTMDs in children and adolescents heading for orthodontic treatment.

Method: Patients between 7 and 18 years (n = 114) heading for orthodontic treatment were included. The diagnostic process consisted of anamnestic examination in line with guidelines of IHS/IASP and functional examination by EACD and AAOP. Patients were divided into four groups depending on the presence of: muscular, muscular and articular pain in the trigeminal region, muscular/

articular pain accompanied by temporomandibular joint (TMJ) sounds, TMJ sounds without pain. In all patients panoramic X-ray was taken. A correlation between aforementioned signs/symptoms and TTH was analyzed.

Results: There was a positive relationship between muscular pain in the trigeminal system and TTH. No significant correlation between TMJ sounds and TTH was found. The relationship between pain accompanied by TMJ sounds and TTH was unclear.

Conclusions: The results may implicate the obligation for the differentiation between various forms of TMDs. The presented study stress the need for further investigation in children/adolescents afflicted by TTH andTMDs.

PO375

Headache disorders in children and adolescents

Types of visual aura seen in children with migraine

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We did an observational study looking at types of visual aura in children with migraine. Our study included 304 patients (177 females with an average age of 12.1 years), with migraine and visual aura. Out of these, 173 (57%) of patients had typical migraine visual aura. The remaining 131 (43%) patients had atypical visual aura. This study provides further evidence supporting that, migraine visual aura could have a variation in duration, character of colours and forms.

PO376

Headache disorders in children and adolescents

Biofeedback-based heart rate variability therapy in adolescents with tension type headache – own experience

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Background: Tension type headache – the most common form of primary cephalgia in children and adolescents. Psychotropic drugs are effectively used in adult patients, but cannot be widely used in pediatric patients due to side effects. Non-drug therapy in this situation is the option of choice.

Aim: To assess the effects of biofeedback-based heart rate variability on functional state in adolescents with tension type headache based on data of clinical studies and neuropsychological analysis.

Methods: 60 adolescents (ages 13–18) were examined. Two groups: experimental group received drug therapy and biofeedback (40 pers.) and control group received only medical therapy (20 pers.) were formed. Reactive and personal anxiety was assessed by the self-esteem scale Spielberger-Hanina, the level of depression was measured on a scale of V.A. Zhmurova in author revision V.V. Boyko. The intensity of pain was assessed by visual analogue scale. Biofeedback was selected to the regulation of psychophysiological state based heart rate variability with automatic calculation of the individual program breathing mode biofeedback.

Results: It was revealed that adolescents with tension-type headache, who received biofeedback in complex therapy showed more significant changes in the studied parameters compared to the patients control group. Efficiency of biofeedback treatment was shown in a clinical improvement of the patient's health and objective indicators of the functional state and adaptive capabilities.

Conclusion: Biofeedback-based heart rate variability characterized by high efficiency in the treatment of tension headache in adolescents. Clinical outcome is accompanied by improvement of the psychological state of patients.

PO377

Headache disorders in children and adolescents

Comorbid disorders and the quality of life in children and adolescents with primary headaches

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In order to assess comorbid disorders, their impact on the course of headaches, and quality of life (QL) were examined using questionnaires and neuropsychological methods 279 children and adolescents with tension-type headache, 164 with migraine and 60 healthy controls. The spectrum and severity of comorbid psychosomatic disorders (anxiety, depression, autonomic dysfunction, fatigue, insomnia, cognitive dysfunction) depend on the frequency of headache. In patients with chronic headache, especially

teenagers, have expressed anxiety, autonomic disorders, mild depression, insomnia, asthenia, and cognitive disorders, often associated with each other. Dissatisfaction with current life situation noted 95,5% of the patients with chronic headache, increased anxiety and depression – 90,9%, reduction in daily activity – 63,3%, reduction of self-control – 54,5%, a reduction of social contacts – 36,4%, worsening of the relation with parents – 31,8%. Quality of life due to the mutual influence of many medical and social factors: the frequency and intensity of headache, severity of emotional disturbances, personality characteristics, family microclimate, level of social adaptation. Established reliable relationship of comorbid disorders among themselves and with quantitative indicators of pain, a significant impact on QL of children and adolescents: in the same form of headache the patients with comorbidity had worse indicators of QL, especially physical activity, emotional well-being, social functioning. With the development of integrated rehabilitation programs for children and adolescents with primary headache the need to pay special attention to the identification and correction of comorbid psychosomatic disorders.

PO378

Headache disorders in children and adolescents

Correlation between characteristics of cyclic vomiting syndrome and levels of adrenocorticotropic hormone and/or antidiuretic hormone

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Background: Cyclic vomiting syndrome (CVS) is characterized by recurrent, stereotypic episodes of incapacitating vomiting. Abnormally high levels of adrenocorticotropic hormone (ACTH) and/or antidiuretic hormone (ADH) have been observed during CVS attacks.

Aim: We evaluated the relationship between various CVS characteristics and ACTH/ADH levels.

Methods: We evaluated data of 31 CVS patients admitted to Teikyo University Hospital. Data collected were age of onset, age of at last attack, duration of CVS, interval of between attacks, duration of attack, ACTH, and ADH levels, and other CVS symptoms. Comparisons were performed using Spearman"s rank correlation coefficient and Wilcoxon rank-sum test, as applicable.

Results: In 25 patients for whom ACTH/ADH data were available, abnormally high ACTH and ADH levels in 17 and 18 cases, respectively. Strong correlations were found between ACTH and ADH values (correlation coefficient: 0.7655 and $p < 0.0001$). The following correlations were also significant: age at last attack and duration of CVS (correlation coefficient: 0.6593, $p = 0.0001$), duration of attack and ACTH values (correlation coefficient: 0.5153, $p = 0.0084$), duration of attack and ADH values (correlation coefficient: 0.5666, $p = 0.0031$), and age at onset and duration of attack (correlation coefficient: −0.4113, $p = 0.0215$). Other symptoms, including bilious vomiting, bloody vomiting, lethargy, pallor, abdominal pain, diarrhea, and headache, were observed in 5, 8, 11, 14, 23, 10, and 18 of 31 cases, respectively. ADH values in patients with bilious vomiting were higher than in those without bilious vomiting ($p = 0.048$).

Conclusions: Duration of attack was correlated to ACTH and ADH values. Thus, abnormally high ACTH / ADH values may indicate severe CVS.

PO379

Headache disorders in children and adolescents

A study on treatment options and prognosis of cyclic vomiting syndrome

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Background: Cyclic vomiting syndrome (CVS) has been classified as a subgroup of migraine.

Aim: We aimed to evaluate the prophylactic use of drugs for the management of patients with CVS.

Methods: This study included 31 patients with CVS who were admitted to Teikyo University Hospital. Eighteen patients underwent prophylactic therapy, while 13 did not. Informed consent was obtained and the Teikyo University Ethics Committee approved the study.

Results: The median frequencies of CVS with or without prophylactic therapy were 0.75 and 0.33 per month, respectively. CVS attacks were more frequent among patients undergoing prophylactic therapy than among those who did not ($P = 0.045$). The median duration of CVS was significantly higher in patients with prophylactic therapy than in those without it (93 vs. 36 months, $P = 0.0033$). Effective treatments were valproic acid, valproic acid with phenobarbital, phenobarbital, and

amitriptyline (9, 4, 3, and 1 cases, respectively). Of 18 patients who underwent prophylactic therapy, one was nonresponsive. Of 17 patients who were responsive, 3 were transferred to another hospital and followed-up and 14 were followed-up in our hospital. Of 14 patients, 13 discontinued drugs and one continued drugs. Regarding valproic acid mono therapy, 6/9 responders and 1/6 non responders had a family history of migraine. The efficacy of valproic acid monotherapy was higher among nonresponders with a family history of migraine compared with those without it ($P = 0.049$).

Conclusion: Prophylactic therapy for CVS was useful for patients with frequent attacks and for those with a long-term history of CVS.

PO380

Headache disorders in children and adolescents

Migraine is associated with bulimia in adolescents

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Background: Although previous studies have shown a relationship between migraine and bulimia, in a specific population of adult women, the authors find no studies that have shown this association in adolescents.

Aims: To verify the association between migraine and bulimia in adolescents.

Methods: A cross-sectional analytic study was conducted among 607 adolescents (388 girls), from public schools, aged between 11 and 18 years, mean 13.9 (CI 13.7; 14.0), carried out between February 2013 and November 2014. The Edinburgh Bulimic Investigatory Test was used to diagnose bulimia. The ICHD-III beta criteria were used for the classification of headache presented by the students. In this study the authors considered as migraineurs individuals fulfilling the criteria of probable migraine and those with tension-type headache coexisting with migraine.

Results: 221/607 (36.4%) adolescents presented bulimia [162/388 (41.8%) girls *vs.* 59/210 (26.9%) boys, $p < 0.05$; X^2]. 217/221 adolescents with bulimia 217 (98.2%) complained of headache. Of these students with headache, 104 (47.9%) had migraine, 55 (25.3%) probable migraine, 19 (8.8%) both migraine and tension-type headache, 24 (11.1%) tension-type headache and 15 (6.9%) headache not classified using the ICHD-III criteria. 454/607 (74.8%) adolescents had migraine [309/388 (79.6%) girls *vs.* 145/219 (66.2%) boys, $p = 0.000$; X^2]. In the multivariate analysis, girls with migraine have 43.7% chance of developing bulimia nervosa [gender female ($OR_{adjusted} = 1.85$; 95% CI: 1.28 to 2.66, $p < 0.01$) and migraine ($OR_{adjusted} = 1.51$; 95% CI: 1.0 to 2.26, $p = 0.048$)].

Conclusion: Girls with migraine present more probability of developing bulimia nervosa.

PO381

Headache disorders in children and adolescents

Autonomic nervous system function in children and adolescents with primary headache disorders

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Symptoms of autonomic dysfunction in pediatric patients with headache are under-recognized and incompletely characterized. Such symptoms, including nausea, vertigo, near-syncope, and disordered sleep intensify the morbidity of pediatric headache. We aim to differentiate autonomic function in patients with migraine and tension headache with healthy controls. We hypothesize that an underlying mechanistic process that persists in chronic headache relates to altered autonomic dysfunction due to sympathetic overdrive. We further expect migraine patients to express higher rates of autonomic dysfunction in comparison to tension-type headache patients and controls due to these alterations in brainstem neurophysiology. Our sample size will include 150 participants, consisting of 50 migraine patients, 50 tension-type headache patients, and 50 healthy controls visiting the Pediatric Headache Program at Boston Children's Hospital, ages 8–18 years old. Participants are first administered the Composite Autonomic Symptom Score (COMPASS-31) detailing their autonomic dysfunction (Sletten, Suarez, Low, Mandrekar, & Singer, 2012). The patient then undergoes clinical autonomic testing, in which his or her heart rate is monitored and blood pressure is measured during baseline, deep breathing, Valsalva maneuver, and active standing. We have currently tested 35 patients (68.6% female), with fairly equal distributions of tension-type headache, migraine, and healthy control patients. The COMPASS-31

questionnaire indicates several endorsements of autonomic symptoms among the migraine and tension-type headache groups, including 64% reporting dizziness, 44% reporting frequent sweating, and 84% having difficulties with bright lights. We are in the process of examining our preliminary findings from the clinical autonomic testing portion.

PO382

Headache disorders in children and adolescents

A retrospective review of autonomic nervous system function in children and adolescents with primary headache disorders

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This retrospective study sought to explore the potential relationship between pediatric primary headache disorders and autonomic nervous system functioning by comparing the prevalence of autonomic dysfunction symptoms in a headache group versus a control, non-headache group. The medical records of migraine and tension-type headache (TTH) patients seen at the Pediatric Headache Program at Boston Children's Hospital (BCH) were reviewed and compared against those records of (control) patients diagnosed with idiopathic scoliosis in the Orthopedic Clinic at BCH. The headache group contained 125 individuals (56.8% female; mean age of 13.9 years; 54.4% diagnosed with migraine), while the control group included 106 patients (68.8% female; mean age of 12.6 years). The presence of autonomic dysfunction symptoms was extracted from the patient's clinical data recorded during initial evaluation. Flagged symptoms included constipation, insomnia, dizziness/orthostasis, blurry vision, hyperhidrosis/excessive cold in hands or feet, and abnormal blood pressure. The combined headache group presented with significantly more dysautonomia than the control group, with the 'hyperhidrosis/excessive cold in hands and feet" symptom being endorsed most frequently, and 'abnormal blood pressure" the least. The TTH group presented with significantly higher dysautonomia compared to the control group in five of the six flagged symptoms (all except 'abnormal blood pressure"), while the migraine group endorsed more dysautonomia symptoms in three of the six domains. When comparing within the headache group (migraine versus TTH), TTH presented with significantly greater dysautonomia in regards to 'blurry vision" and 'hyperhidrosis/excessive cold in extremities.".

PO383

Headache disorders in children and adolescents

Spatial attention effect on sep components differentiates migraine children with imploding pain from those with exploding pain

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Objectives: Different pathophysiological mechanisms have been demonstrated in young migraineurs with either imploding (IP) or exploding (EP) pain (Iacovelli et al., 2013). Our aim was to investigate whether the effect of spatial attention on SEPs is different between IP and EP migraineurs.

Methods: We studied 10 IP migraineurs and 9 EP migraine children. SEPs to median nerve stimulation were recorded from 31 scalp electrodes in a neutral condition (NC) and in a spatial attention condition (SAC), in which subject had to count tactile stimuli delivered on the stimulated hand.

Results: In the frontal region the N140 amplitude increase in SAC was higher in EP than IP migraineurs ($F = 6.41$, $p = 0.01$). In both NC ($F = 15$, $p < 0.001$) and SAC ($F = 10.2$, $p = 0.001$), the N140 latency was shorter in IP than in EP patients. In NC, the N120 latency was shorter in IP than in EP migraineurs ($F = 6.5$, $p = 0.01$). In EP patients, but not in IP migraineurs, the P100 latency was shorter in SAC than in NC ($p = 0.04$).

Conclusions: Our results suggest that the psychophysiological mechanisms underlying spatial attention are different in migraine children with imploding or exploding pain.

Key message: This study confirms that pain directionality represents an important phenotypic aspect of pediatric migraine.

PO384

Headache disorders in children and adolescents

Correlation between abnormal brain excitability, anger management and anxiety in migraine children

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Objective: To analyze the possible correlation between abnormal brain excitability and psychological factors in migraine children.

Methods: We studied 12 migraine children. Auditory event-related potentials (ERPs) were recorded in three successive blocks to test habituation. Psychological profile was assessed by Picture Frustration Study test for anger management (PFS) and Psychiatric scales for self-administration for youths and adolescents (SAFA-A scale for anxiety).

Results: In migraineurs, all the ERP components (N1, P2, and P300) showed a reduced habituation, as compared to healthy children. In both the second and third blocks, a significant correlation between P300 deficit habituation and SAFA-A (social anxiety subscale) was found. Moreover, the P300 habituation was also correlated with PFS-I (intraggressive anger) in the second block and with the total SAFA-A score in the third block.

Conclusions: To our knowledge, this is the first study showing a correlation between abnormal brain excitability, intraggressive anger and anxiety, suggesting a possible role of the latters in producing the migraine phenotype in children.

Key message: Our results confirm our previous study (Valeriani et al., 2009) showing that in pediatric age neurophysiological abnormalities, linked to the genetic background of migraine, and psychological features concur in determining the migrainous phenotype.

PO385

Headache disorders in children and adolescents

Chronic migraine: does chronicity affects phenotype of headache?

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Aim: Migraine is a chronic disorder characterized by moderate-severe headaches and a major public problem for all continents, and drains patients energy and working capability. Prevalence of migraine in Turkey was reported 16,4% and chronic migraine consisted 10% percent of this patients. Chronic migraine (CM) is challenging for clinicians and closely related with disability of patients.

Method: The study consisted of patients admitted to tertiary headache database electronically. Database comprised by 3847 patients and 589 of them were CM patients, sociodemografic features and clinical characteristics assesed in this study

Results: Fifteen (15%) percent of migraineurs were chronic migraine patients. Study group were consisted 507 women and 82 men (% 86,1 &%13,9). CM group median values; 38 (9–75), disease duration 60 months (12–120), headache frequency 25 days/month (16–30), headache duration 12 hours (4–24), headache severity 8 (VAS) found. Throbbing headache (71,3 percent) reported as most frequent headache pattern, and followed by tension (16,9 percent) and doll headache (7,6 percent) patterns. Localization; unilateral at 38,1 percent, and followed by generalized, occipital. Intraday course of headache evaluated; 36,5 percent of patient's headache were prominent in the evening, 26,5 percent of patients reported headache equally for daylong. Interestingly 14,1 percent of patients reported awakining headache.

Conclusion: CM is a condition that phenotype of pain is affected by the course of chronification and is an important health issue for population and patient life. Population based broad studies are necessary to reveal association of enviromental, age and sex related factors on phenotypic presentation.

PO386

Headache disorders in children and adolescents

Migraine in preschool age children: a comparison with older children

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Background: Although migraine frequency is increasing in preschool age children, an extensive evaluation of the clinical features in affected subjects has yet to be achieved.

Aim: The aim of the present study was to evaluate and compare some features of migraine phenotype of two different paediatric age groups of affected patients (under vs. over 7 years old)

Method: In this retrospective study we analyzed all standard clinical files of children with diagnosis of primary headache, collected for 4 years, included all children under 7 years old with diagnosis of migraine. We reported twenty clinical variables for each participants.

Results: The sample was composed of 374 children (approximately 50% males and females) affected by migraine with/without aura. About 9% of them were affected by preschool migraine (<7 years old). No significant statistical differences were found, except for the shorter history of disease, the reduced frequency of attacks, and the shorter duration of episodes compared to older children.

Conclusion: Features of migraine in preschool age children were fairly similar to those of older children, including similar frequencies of osmophobia, allodynia, and cranial autonomic symptoms. However, different modules result activated with different clinical expressions intra age but not inter age.

PO387

Headache disorders in children and adolescents

Comorbidity in childhood headache: a case report of a rare condition of migraine without and with aura and intra/extracranial malformation

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Backgrounds: In children, the diagnosis of stroke caused by migraine is still questioned. The arterial ischemic stroke comprises the 5–10% of all pediatric strokes.

Aim: We described a male patient of 12 y.o, with a pathological anamnesis, of 4 years of headhache attacks. A white light was reffered in both eyes lasting few minutes. Recently he presented an «amaurosis fugax», lasting few minutes, with asthenia but not headache. He had a first line familiarity for Headache, Cardiovascular Diseases, Metabolic Diseases.

Methods: Because of the extremely high cardiovascular diseases' familiarity, Thrombophilia risk was evaluated by Blood and Genetic exams; ECG; Ecocardiography; Epiaortic Echo-doppler.

Results: A heterozygosis for MTHFR resulted. Echo-Doppler showed a calibre riduction (Dx:7.8 mm vs Sn:4.5 mm) of the Left Common Carotid Artery and in the left external branch. By Angio-MR without CM, no Carotid Artery on Left and aberrant tangle of vases were showed. The Angio CT with MDC and VTR intracranic presented: an hypoplasia of the Left Common Carotid artery, the I.C. Agenesy and absence of carotideal channel inside the petrosus rocca Temporalys.

Discussion: The differential diagnosis was among a Secundary Headache or a Primary one. The exam results gave evidence to a rare pathology of Internal Carotid Agenesia (prevalence < 0,01%). Thus, the diagnosis was of Migraine without and with Aura and Intra/Extracranial Malformation, of the Type D of Carotid Anomaly.

Conclusions: The headache could be an epiphenomenon of a myriad of secondary causes. If «amaurosys fugax» is presented, we should exclude an association with secondary headache.

PO388

Headache disorders in children and adolescents

The headache in children with epileptic encephalopathy

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Introduction: Epileptic encephalopathy – is a condition where abnormal electrogenesis of brain is the cause of disorders of the brain functions. In this condition the epileptic process itself leads to progressive brain damages.

Aim of the study. To study the features of neurological status in children with epileptic encephalopathy and to find the characteristics of headache in paediatric patients with epileptic encephalopathy.

Materials and Methods: We studied 120 children aged from 3 to 14 years, diagnosed with epileptic encephalopathy. We studied children using standard protocol: neurological examinations, Electroencephalography (EEG), and Magnetic resonance imaging.

The results of the study: All of them were suffering by acute or chronic headache and symptomatic epilepsy. Preictal headache was present in 12 (10%) patients, postictal in 30 (25%) and interictal in 60 (50%) patients. Among the patients with postictal headache 10 (33.3%) had migraine, 15 (50%) tension -type of headache and 5 (16.7%) other headaches. The study of neurological patients with epileptic encephalopathy revealed the

prevalence of cognitive impairment, decreased intelligence, memory and thinking.

Conclusion: Thus, a detailed clinical and neurological analysis of patients correlated with EEG data allowed to exclude the incorrect diagnostics of epileptic encephalopathy in children. Among the patients with symptomatic epilepsy interictal migraine was commonly than other headaches.

PO389

Headache disorders in children and adolescents

The relationship between headache and abnormal EEG findings in children with symptomatic epilepsy

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Introduction: Epilepsy is one of the most complex medical and social problem at present time. Headache is a main symptom that occur before or after epileptic seizures. It has been stated that headache may represent an epileptic event. EEG abnormality is a prominent finding in children with headache.

Aim: The aim of this study was to evaluate EEG abnormalities in children with symptomatic epilepsy on the background of headache.

Materials and methods:: We studied 119 children aged from 3 to 14 years, 69 of them were diagnosed with epileptic encephalopathy and 50 with symptomatic epilepsy. In this study we used clinical, neurological and instrumental methods of investigation such as EEG (electroencephalography).

Results: The study of neurological patients with epileptic encephalopathy revealed the prevalence of cognitive impairment, decreased intelligence, memory and thinking. In neurological status of patients with symptomatic epilepsy it is often revealed the predominance of focal neurological symptoms. Comparing EEG abnormalities in different types of headache revealed that there is an association between them. There was also a significant difference between EEG abnormalities in different types of aura. headache mainly was associated with the children's age.

Conclusions: Our study disclosed headache as a common symptom in children with symptomatic epilepsy. headache and abnormal EEG findings are significantly associated. Thus, a detailed clinical and neurological analysis of patients allowed us to establish the main of cause headache in children.

PO390

Headache disorders in children and adolescents

The effect of the virtual interactions on well-being in adolescence: exploring the relationship between internet addiction, headache and depressive symptoms

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Background: The excessive use of internet is considered to have a negative impact on physical health, leading to physical symptoms, like headaches. Furthermore there is evidence suggesting that the use of the internet is associated with psychopathological risk, especially depressive symptoms in adolescents.

Aim: To explore the relationship between primary headache, migraine (M) vs tension type (TTH), internet addiction and depression in a non clinical population of adolescents.

Method: 240 Italian middle school students (Males = 115, 47.9%; Females = 124, 51.7%; 1 missing; mean age = 11.8; SD = .97) completed the self-report measures*: Headache Clinical Record*, in according to the ICHD-2 (2004); *Internet Addiction Test (IAT)* assessing internet addiction; *Children's Depression Inventory (CDI)* assessing depressive symptoms.

Results: About 28.0% of participants (N = 67) declared headache (Males = 10%; Females = 18.0%). No prevalence of a headache type among Internet abusers emerged. Depressive symptomatology of participants with M or TTH and classified as "problematic or addicted Internet user" was compared to that of participants with M or TTH and classified as "below or on average Internet users". The t-test resulted barely significant (t-test(61) = 1.73, $p = 0.09$, Cohen $d = 0.44$) with the "problematic or addicted Internet user" group reporting the higher means. Correlations among M and TTH and Internet addiction and Depressive symptomatology were performed. M correlated positively with CDI scores ($r = 0.138$, $p < 0.05$).

Conclusion: The associations between primary headache, internet addiction and emotional distress should be further explored in prospective studies to better understand their effect on psysical and emotional well-being.

PO391

Headache disorders in children and adolescents

Anxiety disorders in children and adolescents with migraine

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Background: Migraine in adult patients is commonly associated with anxiety and depression – in 30–40% [Jette N., 2008]. Anxiety, more than depression, predicts long-term migraine persistence, headache-related disability and reduces the efficacy of treatment. [Lantéri-Minet M, et al., 2005]

Aim: To assess the incidence of anxiety disorders (AD) in children and adolescents suffering migraine.

Method: 187 children and adolescents aged 7–16 years with migraine established by the diagnostic criteria of ICHD-2 were included into the study. AD were diagnosed according to the ICD-10 diagnostic criteria. The severity of AD was evaluated with the Spence Children's Anxiety Scale [Spence S.H., 2003].

Results: The manifestations of AD were revealed in 86 (46%) of migraine patients. The severity of AD was graded as mild in 56 (49%), moderate in 37 (32%) and marked in 16 (19%) of cases. Generalized AD was diagnosed in 12%, social AD in 33% and different phobias in 55% of cases.

The frequency and severity of migraine attacks were the most prominent in patients with co-morbid generalized AD. On average the attacks frequency was $4{,}8 \pm 2{,}3$ in a month in migraine patients with co-morbid AD compared with $2{,}1 \pm 1{,}8$ in migraine patients without AD ($p < 0{,}01$). The attacks were often provoked by emotional or stressful events.

Conclusion: Diagnosing the **c**o-morbid AD is an important factor for planning the treatment of migraine in children and adolescents. Successful management of AD contributes to alleviation the frequency and severity of migraine attacks, as well as reducing the risk of migraine transformation into it's chronic form.

PO392

Headache disorders in children and adolescents

Psychosocial and demographic characteristics of children with migraine presenting for infusion treatment

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Background: Headache infusion centers are designed to treat refractory migraine in an outpatient office rather than in the emergency department. Few infusion centers dedicated to pediatric migraine currently exist and there is limited data on demographics and characteristics of children utilizing these services.

Aim: To identify demographic variables of children with migraine presenting for treatment in an outpatient pediatric infusion center. To identify psychosocial variables (quality of life, functional disability, coping, emotional and behavioral concerns) associated with treatment in the infusion center compared to children with migraine (age and gender-matched) not receiving infusion treatment.

Method: A retrospective chart review of children with migraine receiving treatment (IV tx group) through the outpatient infusion center from June to December 2014. To examine differences between psychosocial variables and infusion treatment, data from participants seen by the first author for bio-behavioral evaluation/treatment of migraine (IV-BH tx group) will be analyzed by matching this group to children with migraine who completed bio-behavioral treatment but did not receive infusion therapy (BH tx group).

Results: Preliminary analyses indicate better psychosocial functioning (quality of life, functional disability) in the IV-BH tx group compared to the BH tx group (all p's $< .05$).

Conclusion: Preliminary results indicate significant differences in demographic and psychosocial characteristics of children accessing infusion therapy for migraine. Further research is needed to better understand the needs of this population.

PO393

Headache disorders in children and adolescents

"Back to school": an educational collaboration and tool for school nurses and their students with headache, migraines, and concussion

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In recent decades, the number of children with chronic illnesses transitioning back to school has increased (Kliebenstein & Broome, 2000). Of the approximately 20% of all children suffering from a chronic illness, about one-third of that number experiences consequences severe enough to interfere with school functioning and performance (Kaffenberger, 2006). Chronic headache is often associated with significant impairment of daily functioning, including difficulty with school performance and attendance (Hershey & Winner, 2007) and higher rates of school absenteeism than children with other chronic illnesses (Powers et al., 2006). School nurses are key players in the school reintegration process, yet some lack the necessary educational resources. This study consists of two phases addressing the necessity, implementation, and efficacy of an educational tool designed for school nurses in supporting the complex needs of chronic pain patients reentering school. Phase I of the study surveyed a total of 73 child and adolescent patients and their parent(s). When asking school nurses whether they would be interested in access to an educational tool, 66.7% of the nurses responded "yes." Phase II of the study focused on the efficacy of the tool from the perspectives of 25 school nurses. School nurses rated the guide a 4.46 out of 5 possible points. Through the development and implementation of an educational tool available to school nurses, this study sought to bridge the gap between initial care and successful reintegration into school for chronic pediatric headache patients.

PO394

Headache pathophysiology and imaging

Utility of sympathetic skin response in the diagnosis and differential diagnosis of migraine, tensión-type headache and fibromialgia

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Objetive: To investigate changes in autonomic function (sympathetic nervoussystem) in patients with migraine, tensión-type headache and fibromialgia,using Sympathetic Skin Response (SSR) and comparing them to 100 controls.

Material and Methods: 100 migraine patients, 50 tension-type headache patients, 50 fibromialgia patients and 21 fibromialgia and migraine patients. Informedconsent was obtained. Autonomic test was done in intercritic phase and without medication. Latency, amplitudes and persistence where recorded. SSR was performed estimulating in glabella and recording from palm and dorsum of both hands. An average statistic studywas done measuring age, gender, side-to-side comparison and controls versus-patients comparison.

Results: There were no differences in age, gender, side-to-side comparison neither in localization of the migraine. We found statistically significant diferences in latency, amplitude and persistente between controls vs migraine, controls vsfibromialgia, controls vs tensión-type headache and also among patients.

Conclusions: SSR is an objective test, reproductible,measurable, easy to perform and no painless to patient. In migraine this study confirms the implication of the autonomic sympatetic nervous system in its generation (hypofunction) and a hyperfunction, hypofunction or both intensión-type headache and fibromialgia.

Note: this work has been partially fundedby FIB (Fondo de Investigación Biomédica) del Hospital Universitario laPrincesa, Madrid.

PO395

Headache pathophysiology and imaging

Structural-metabolic abnormalities of brain regions on migraine realization

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The purpose of our study is the investigation of white matter tracts damages and neurometabolites with estimation of theirs part in different types of migraine realization.

Material and methods: There were examined of 67 patients with migraine and 22 healthy volunteers by DTI with tractography. Analysis of fractional anisotropy (FA) and mean diffusivity (MD) was performed. Multivoxels[1] H-MRS was obtained at 18 patients with migraine (voxels

of frontal, temporal and occipital lobes, thalamus, girus cinguli, hippocampus). Electroencephalographic mapping was performed for all patients (Neirosoft, Russia).

Results: Subjects with migraine, as compared to healthy controls, demonstrated abnormal parameters of FA and MD ($p < 0.05$). Patients with migraine without aura (MWA) have significance decreasing of FA in anterior brain regions (frontal and temporal parts) and MD increasing in posterior regions.

Patients with MWA have reducing of tracts visualization in occipital lobe and absence of posterior commissure. There were EEG-photoparoxysmal patterns registrated at those patients.

DTI in cases of migraine with aura (MA) detected of FA decreasing and MD increasing in *corona radiata* ($p < 0.05$) with reducing of tracts visualization in *corona radiata* and hippocampal areas. Paroxysmal EEG-activity dominated in temporo-occipital areas.

Neurometabolites ratio NAA/(Cho + Cr) was decreasing (from 0.29 to 0.64) in hippocampal, occipital and thalamus voxels in MA. In cases of MWA decreasing of all metabolites concentrations was found into voxels of girus cinguli and frontal lobe.

Conclusion: DTI with tractography and ^{1}H-MRS data are anatomic correlates of migraine course. Degree of metabolic abnormalities correlated with frequency of migraine attacks.

PO396

Headache pathophysiology and imaging

Rhinogenic contact point headache: a review of imaging findings

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Objective: To define anatomical abnormalities that may lead to rhinogenic contact point headache.

Methods: Paranasal sinuses CT scans and medical records of one hundred patients who underwent a successful endoscopic surgery for rhinogenic contact point headache reviewed.

Results: Eleven distinct anatomical abnormalities were found in patients with rhinogenic contact point headache involving different sites of the nose and paranasal sinuses including nasal septum, superior and middle turbinates and ethmoidal sinuses.

Conclusion: There are multiple anatomical situations that may lead to rhinogenic contact point headache. The CT scan of patients must be reviewed carefully to find the underlying abnormality which may lead to rhinogenic headache even in the absence of a distinct sino-nasal inflammation. Treatment plan should be personalized for every patient considering the diagnosed anatomical variation.

PO397

Headache pathophysiology and imaging

Low heat pain thresholds in migraineurs between attacks

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Background and Objective: Between migraine attacks, migraine is associated with hypersensitivities to sensory stimuli such as lights, sounds, odors and stimulation of the skin. The objective of this study was to investigate hypersensitivity to heat pain in migraineurs between attacks.

Methods: Cutaneous heat pain thresholds were determined for 112 migraineurs who had been migraine attack free for at least 48 hours and for 75 healthy controls. Pain thresholds at the forehead and forearm were compared between migraineurs and controls using two-tailed t-tests. Amongst the migraineurs, correlations between pain thresholds and number of hours until the next migraine attack, headache frequency, and allodynia symptom severity were calculated.

Results: Migraineurs had lower pain thresholds than controls at the forehead ($43.9^\circ C +/- 3.2^\circ C$ vs. $45.1^\circ C +/- 3.0^\circ C$, $p = .015$) and at the forearm ($43.2^\circ C +/- 3.4^\circ C$ vs. $44.8^\circ C +/- 3.3^\circ C$, $p < .001$). There were not significant correlations between heat pain thresholds and headache frequency or allodynia symptom severity. For the 41 migraineurs for whom the number of hours until their next migraine attack was known, there were positive correlations between the time until the next headache and pain thresholds at the forehead ($r = .352$, $p = .024$) and forearm ($r = .312$, $p = .047$).

Conclusions: Between migraine attacks, migraineurs have lower cutaneous heat pain thresholds than healthy controls. Positive correlations between pain thresholds and time to next migraine attack suggest that mechanisms

underlying these lower pain thresholds also predispose the migraineur to their next migraine attack or that the low pain threshold is an early sign of the migraine attack itself.

PO398

Headache pathophysiology and imaging

Contribution of intrinsically photosensitive retinal Ganglion cells in the photophobia of migraine patients

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Background: It has beenreported that the intrinsically photosensitive retinal ganglion cells (ipRGCs) areinvolved with migraine headache caused by the photophobia, based on a researchin which photosensitive tests induced headache attacks in migraine patientswith damaged cones/rods and normal ipRGCs.

Aim: This study aimed to elucidate the effect of ipRGCs in photosensitivity experiences of migraine patients with normal vision.

Method: The subjects were 30 migraine patients and 30 normal controls. The subjects rated the discomfort of the glare under four kinds of light source condition. Stimulations from light source 1 (LS-1) for S, M, L cones, and ipRGCs were each defined as100 each and those from the other light sources were calibrated relative to LS-1: for LS-2 and LS-3, ipRGCs stimulations were set at 80 and 62; and for LS-4, cone stimulations were set differently from LS-1 (S: 185, M: 107, L: 95).

Results: No differences were observed in discomfort glare estimation between the migraine group and normal control group for any of the four light sources. Within the migrainegroup, discomfort glare from LS-4 was higher than that from LS-1and LS-2 with low luminance.

Conclusion: In migraine patients, no differences were noted in discomfort glare among different levels of ipRGCs stimulation. However, the light sources with higherlevels of S-cone stimulation may produce more severe discomfort glare, which indicates that the difference in colors (blue light) might play a critical rolein causing discomfort glare.

PO399

Headache pathophysiology and imaging

Gray matter changes related to medication overuse in patients with chronic migraine

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Objective: To investigate the neurological substrate associated with medication overuse (MO) in patients with chronic migraine (CM).

Methods: We recruited age- and gender-matched patients with CM with and without MO and healthy controls (HCs). Demographics and headache characteristics were recorded before the patients underwent magnetic resonance imaging. T1-weighted images were processed by voxel-based morphometry, and the findings were correlated with clinical variables, including treatment responses.

Results: A total of 66 patients with CM (half with MO) and 33 HCs completed the study. Patients with CM with MO compared to the patients without MO showed a gray matter volume (GMV) decrease in the bilateral rectal gyrus of the orbitofrontal cortex (OFC) and left middle occipital gyrus as well as an increase in the GMV in the left temporal pole/parahippocampus. The GMV differences were correlated with the frequency of analgesics use (OFC: $r = -0.344$, $p = 0.005$; left middle occipital gyrus: $r = -0.367$, $p = 0.003$; left temporal pole/parahippocampus: $r = 0.364$, $p = 0.003$). The changes in these three brain regions explained 28.4% variance of the analgesics use frequency, after controlling for demographic and clinical variables. The patients who responded to treatment had a greater GMV in the OFC ($p = 0.030$).

Conclusion: Our study showed GMV changes in CM patients with MO compared to the patients without MO. These three cerebral regions accounted for significant variance in the analgesics use frequency. Moreover, the GMV of the OFC was also predictive of the response to MO treatments.

PO400

Headache pathophysiology and imaging

Interictal hyper-responsiveness in flash visual evoked potentials of migraine patients

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Background: Pattern-reversal visual evoked potentials (PRVEPs) in migraine showed variable results, but Flash visual evoked potentials (FVEPs) in migraine showed usually in the increased amplitude. We have tried to ascertain whether the amplitude of FVEPs increase and the other abnormality of FVEP present.

Methods: FVEPs were recorded in 25 patients with migraine with aura, 23 patients with migraine without aura during interictal period without specific medications associated with migaine and 48 normal subjects. The migraine groups consisted of 11 men and 14 women in migraine with aura patients aged 20 to 71 years (mean age; 49 years), and 12men and 11 women in migraine without aura patients aged 27 to 70 years (mean age; 57 years). The normal control group consisted of 23 men and 25 women in healthy volunteers aged 28 to 71 years (mean age; 54 years).

Results: The amplitude of FVEPs in migraine showed significant increase ($p < 0.001$) compared to normal subject, and only A1(N1-P1) amplitude in migraine without aura showed significant increase ($P < 0.05$) compared to migraine with aura.

Conclusion: The increased amplitude of FVEPs compared to PRVEPs results in other study suggest that migraine brain is more excitable in flash stimulation associated Y-system than pattern stimulation associated with X-system. These findings are explained by specific cortical distribution of serotonin and noradrenaline in X,Y-system of the visual cortex.

PO401

Headache pathophysiology and imaging

Somatosensory evoked potentials of brain in chronic migraine

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Background: Significance of the central structures of the nervous system which participate in the nociceptive information processing, still remains to be solved in chronic migraine.

Objective: To study the peculiarities of somatosensory evoked potentials (SEPs) in chronic migraine.

Methods: Patients identified as chronic migraine sufferers according to the ICHD-3 beta offers criteria. SEPs were recorded in 25 patients with chronic migraine (21 females, 4 males, mean age 35 y. $\pm$ 11 s.d). The control group consisted of 15 healthy volunteers. SEPs registration was performed in response to electrical stimulation of the median nerve on the wrist. Capacity index (mv x ms) was applied for evaluation of the SEPs late components. It was calculated as an area under the SEPs curve at the interval of 100–600 ms.

Results: Parameters of the SEPs early components (latency $<$ 100 ms) for the chronic migraine patients did not differ from the normal values. A tendency of the amplitude and duration increase was revealed for the SEPs late components (latency $>$ 100 ms). Statistically reliable difference was established for capacity index ($p < 0,05$). Its magnitude exceeded 420 mv x ms in 14 patients. After treatment that difference between the groups was insignificant.

Conclusions: Certain peculiarities of reactivity for the central parts of the sensory analysator exist. Their essence consist in generalization of information about the peripheral nociceptive impulse along the vast associative areas of the cerebral cortex. Data specified can characterize one of the central factors in the mechanism of the chronic migraine development.

PO402

Headache pathophysiology and imaging

Inhibition of entorhinal neural apoptosis and propagation of spreading depression associated by blocking nmda receptor

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Repetitive spreading depression (SD) waves, involving depolarization of neurons and astrocytes and upregulation of glucose consumption, is thought to lower the threshold of neuronal death. N-methyl-D-aspartic acid-receptors (NMDAR) induced a cascade of apoptosis in cell associate by entrance calcium in neurons. NMDARs were enhanced

activity and number in SD induction. Our hypothesis is blocking of NMDAR had neuroprotective and antagonistic roles in repetitive spreading depression. 28 male rats from post-weaning was induction SD by KCl (3 mM; 10–15 μg) once per week at a month. MK-801(antagonist NMDAR) or normal saline was treated 5 minute before SD induction. The percentage of TUNEL positive cell in Entorhinal was significantly decreased after NMDAR antagonist treated ($P < 0.01$), Also the amplitude and frequency of SD waves reduced ($P < 0.05$). The present role of NMDAR, supports the hypothesis of agonistic glutamatergic role on SD waves propagation and neuronal death.

PO403

Headache pathophysiology and imaging

Microglial activation by multiple inductions of cortical spreading depression

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Background and Aim: Cortical spreading depression (CSD) is a slow propagating wave of near-complete depolarization of neural cells that spreads at 2 to 5 mm per minute in the cerebral cortex. CSD is likely to be the biological substrate of migraine aura. Further, multiple CSD occurrences are observed in patients with subarachnoid hemorrhage, malignant stroke, and possibly hemiplegic migraine. Meanwhile, cortical microglia are involved in immune surveillance, and microglial activation leads to brain inflammation. Here, we examined the effect of multiple CSD inductions on the density and morphology of cortical microglia.

Methods: CSD was induced five times by applying 1 M KCl to the cerebral cortex in male C57BL/6 mice. The induction of CSD was monitored by recording DC potentials at an electrode close to the induction site. Mice were sacrificed at either 30 minutes, 3 hours, or 24 hours after CSD. Cortical sections were immunostained for the microglia-specific marker, Iba1. Sham-operated mice were also investigated ($n = 15$ in total). The somal area of Iba1-positive cells was measured using an imaging software. Iba1-postive cell with somal area larger than 70 μm^2 was considered as enlarged microglia.

Results: There was no significant change in the density of microglia after multiple CSD inductions. However, the number of enlarged microglia significantly increased at 24 hours after CSD ($p < 0.01$ vs control). Such hypertrophic changes were not recognized at 30 minutes and 3 hours after CSD.

Conclusion: Multiple CSD inductions cause a delayed activation of resident microglia, which may lead to the development of brain inflammation.

PO404

Headache pathophysiology and imaging

Reversible cerebral vasoconstriction in migraine headaches

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Aim: Study aimed at detection and evaluation of Reversible cerebral vasoconstriction syndrome (RCVS) in Migraine Headache.

Patients and Methods: Totally 48 migraine, female patients, aged 18 to 60 years, with 1–2 attacks per month had been investigated. Control consisted with 15 healthy persons. Patients and control underwent the ultrasound investigations during 2 months. Patients were researched 2 times per month during headache attack and interictal period as well. Controls researched 1 time per month. Sonography examinations performed using Transcranial Dopplerography (TCD) and Transcranial Color-Coded Duplex Sonography (TCCD) methods. Data were calculated by nonparametric Binomial test.

Results: In Migraine patients no correlation was found between site and side of pain and pain intensity. Vasospasm was revealed during severe headache attacks and in interictal period as well in 65% of patients. In these patients the mean flow velocity (MFV) in carotid siphons' (CS) was 74.2 ± 11.8 cm/sec, MFV in middle cerebral arteries' (MCA) amounted 116.4 ± 22.7 cm/sec, MFV in anterior cerebral arteries' (ACA) amounted 101.6 ± 12.8, MVF in Basilar Artery(BA)- amounted 72.6 ± 16.2, averaged Lindegaard Index (LI) was 2.9 ± 0.7 and revealed vasospasm as compared to controls: MFV (MCA) amounted 62.2 ± 8.4 cm/sec, LI (2.1 ± 0.3), $p < 0.001$; The MCA was involved in 18.9% of patients, the ACA- in 12.8%, the PCA- in 28.1% and the BAS- in 40.2% of migraine patients.

Conclusion: Present study showed that vasospasm in migraine headaches is more determined to posterior circulation.

PO405

Headache pathophysiology and imaging

Worsening/improving of headache is related to positional changes in CSF pressure in headache arising from high/low CSF pressure

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Background: The postural headaches are characterized by position-related worsening/improving of pain, but there is not evidence base that this clinical feature is related to positional changes in CSF pressure.

Aim: To test if worsening/improving of postural headache is related to positional changes in CSF pressure.

Methods: We prospectively performed lumbar puncture in order to measure lumbar CSF opening pressures and to monitor, for 1 h through a lumbar needle, the CSF pressure in 37 consecutive headache sufferers with postural headache. During continuous monitoring of CSF pressure, patients were placed before in lateral decubitus for 15 minutes and then in Trendelenburg positioning (TP) for the next 15 minutes in order to record CSF pressure changes.

Results: Of the 37 headaches sufferers with postural headache 18 patients had an elevated CSF opening pressure ($>250\ mmH_2O$) and 10 had a low CSF opening pressure ($<60\ mmH_2O$). Nine patients had a normal CSF opening pressure. TP induced an increase of CSF pressure (mean $\pm$ DS $86{,}2 \pm 15{,}2\ mmH_2O$) and a worsening of headache in patients with elevated CSF pressure, while a less change in CSF pressure associated with improving of pain were observed in patients with low CSF pressure (mean $\pm$ DS, $28 \pm 7{,}1\ mmH_2O$). There was no significant change in CSF pressure during TP in patients with normal CSF pressure.

Conclusion: Changes in CSF pressure are associated with the worsening/improving of the postural headache, suggesting that TP may be useful in diagnostic strategy of headache arising from high/low CSF pressure.

PO406

Headache pathophysiology and imaging

Chronic refractory migraine- the possible role of a parietal dysfunction related to allodynia extent

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Aim: Data regarding PET/TC imaging in migraine (M) are not particularly relevant even if some convergence is now evident. Nevertheless, our aim was to stress possible functional alterations in chronic M refractory to acute and prophylactic therapies.

Methods: Observation started in September 2012. We enrolled 6 subjects (3 males, age 18–33 years), refractory to any therapy, without any psychological disturbances (DMS IV), showing normal MRI. Control group included 6 matched subjects personally and familiarly exempt from any primary pain. We investigated cerebral glucose metabolism using [(18)F]-fluorodeoxyglucose (FDG/TPET-TC) as an index of neural activity, during severest phases of refractory M. Normalized FDG uptake values were calculated with reference to the pons. PET images were analyzed with regions of interest (ROI) and statistical parametric mapping (SPM) approaches. To have a measure of allodynia not only on the cephalic area but all over the body, we used the Dixon up and down method starting with the VF filament 5 (in a standard kit) and then based on the subjects response for moving to next highest filament or the next lowest.

Results: During M attacks, hypometabolism was seen in the parietal cortex and increased simultaneously withe allodynia extent. We have to use or 3 or 2 filament in head area, 3–5 in the body. Memory decrease occurred during attack-phase versus controls and baseline ($p > 0.0001$).

Conclusion: Results indicate a parietal dysfunction likely related to both the extent of allodynia of sufferers from chronic refractory M.

PO407

Headache pathophysiology and imaging

Microembolic signals detection in patients with higher cortical functions impairment during migraine aura

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Introduction: Impairment of higher cortical functions during migraine aura is more frequent than was previously thought. In this study, we aimed to evaluate prevalence and clinical impact of interictal microembolic signals (MES) in migraine patients with higher cortical dysfunction (HCD) during aura.

Methods: Examination was performed over 68 patients, 34 migraineurs with HCD during aura (HCD group) and 31 migraineurs with aura without HCD (Control group I), and 34 healthy controls (Control group II). For microembolic signal detection, the Doppler instrument was used. Demographic data, disease features and MES detection between these groups were analyzed.

Results: Difference in terms of gender, age at the time of examination and age of headache onset was not found. Aura was longer (34.71 ± 18.05 vs. 23.87 ± 13.64, $p = 0.002$) and frequency of aura per year was higher (16.29 ± 14.21 vs. 10.10 ± 11.00, $p = 0.029$) in the HCD group as compared to the Control group I. Also, sensory aura was significantly more present in HCD group ($p < 0.001$). MES were detected in 10 (29.4%) patients from HCD group, which was significantly higher compared to 1 (3.2%) in Control group I and 2 (5.9%) in Control group II ($c2 = 7{,}909$, $p = 0.005$; $c2 = 6{,}476$, $p = 0.011$). Duration of aura, presence of somatosensory aura and presence of MES are identified as independent predictors of the HCD during the aura.

Conclusion: The present findings of high prevalence and frequency of MES in migraine patients with HCD during aura indicate that the relation between HCD and MES exists and requires further investigation.

PO408

Headache pathophysiology and imaging

Investigation of the 5-HT2B receptor in murine primary cells with relevance to a mouse migraine model

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Introduction: Clinical studies revealed that the 5-$HT_{2B/2C}$ agonist *meta*-Chlorophenylpiperazine (mCPP) induces migraine-like headache more likely in migraineurs than in subjects without a history of migraine. These results and the findings from other studies on the serotonin 2B receptor (5-HT_{2B}) give a hint that the receptor may play a role in the pathogenesis of migraine. We therefore developed an animal model for chronic migraine, where we are able to induce a neurogenic inflammation in the dura mater of hypoxic mice with 5-HT_{2B} agonists. This process can be blocked by specific 5-HT_{2B} inhibitors.

Until now, little is known about the 5-HT_{2B} receptor: It seems to be expressed on endothelial cells of blood vessels, but it may also be present on other cell types. Its role in the pain transduction pathway of migraine is not completely clear yet.

Aims: Investigation of the 5-HT_{2B} receptor in a primary cell culture system to determine the location and associated signalling pathways of the receptor.

Methods: Cultivation of primary cells. Immunocytochemistry and Reverse Transcriptase PCR to investigate the cell type which expresses the receptor. Signal transduction assays.

Results: The 5-HT_{2B} receptor is present on endothelial and smooth muscle cells in a dura mater primary culture. Depending on stimulation/-time with 5-HT_{2B} agonists, concentration-dependent signals in 5-HT_{2B} positive primary cells are measurable.

Conclusions: This study revealed the expression and signalling pathways of 5-HT_{2B} receptors in a primary culture system. These results might be well-correlated with the previous findings in the mouse migraine model.

PO409

Headache pathophysiology and imaging

mCPP induces transcytosis at dural blood vessels in a mouse migraine model

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Background: Migraine attacks originate in the meninges which are densely innervated by trigeminal nerve fibers. Upon stimulation, endothelial cells of dural blood vessels secrete nitric oxide and, as a consequence, neuropeptides are released from trigeminal nerve fibers. This, in turn, leads to meningeal plasmaproteinextravasation (PPE) and vasodilation. Inflammatory components such as PPE and vasodilation serve as indicators for migraine attacks in animal models. In our mouse migraine model, the partial 5-$HT_{2B/2C}$ receptor agonist meta-Chlorphenylpiperazine (mCPP) induces PPE in the dura mater of hypoxic mice.

Aim: To identify the part of the vasculature where PPE occurs and the associated cellular mechanism (transcellular vs. paracellular pathway).

Methods: Hypoxic mice received mCPP or Saline, combined with horse radish peroxidase (HRP). Durae matres were prepared for electron microscopy and the endothelium of dural blood vessels was investigated.

Results: After stimulation with mCPP, HRP escaped from capillaries and venules of hypoxic mice. This was evident due to the massive occurrence of HRP-positive vesicles in the endothelium. After stimulation with Saline, HRP-positive vesicles were only present at arterioles.

Conclusion: The PPE is associated with increased transcytosis across the endothelium of dural blood vessels. This finding indicates a transcellular mechanism of permeability.

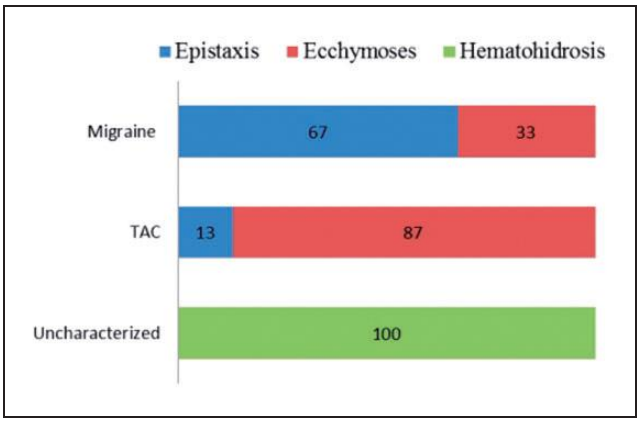

Figure 1. Proportion of Spontaneous Extracranial Hemorrhagic Phenomena (SEHP) among Primary Headache Disorders (PHD). Among patients with SEHP, associated PHDs include migraine and trigeminal autonomic cephalgias (TAC). Epistaxis was the most common hemorrhagic phenomena among migraineurs, whereas ecchymosis was more common among patients with TACs.

PO410

Headache pathophysiology and imaging

Spontaneous extracranial hemorrhagic phenomena in primary headache disorders: a 120-year systematic review and pooled analysis of published case studies

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Background: Head pain is a cardinal feature of primary headache disorders (PHD) oftentimes accompanied by autonomic and vasomotor changes (ICHD-3 beta). Spontaneous extracranial hemorrhagic phenomena (SEHP) as features of PHDs are poorly characterized.

Aim: To critically appraise the association between SEHP, including – epistaxis, ecchymosis, and hematohidrosis – and primary headache disorders, by systematically reviewing all reports of SEHP in headaches and conducting a pooled analysis.

Methods: Advanced search employing PubMed/MEDLINE, Web of Science, and Cochrane Library databases inclusive of relevant grey literature search were employed for clinical studies by combining the terms 'headache AND ecchymosis', 'headache AND epistaxis', and 'headache AND hematohidrosis' spanning all medical literature prior to December 1, 2014. PRISMA and MOOSE guidelines were applied.

Results: A total of 115 cases of SEHP associated with PHDs were identified (median age 27 years, male:female ratio 1:2.3). Among the hemorrhagic phenomena reviewed, 57% were epistaxis, 38% ecchymosis, and 4% hematohidrosis. PHDs reported were migraine with and without aura (83%) and TACs (17%) (Figure 1). Eighty-three% applied ICHD diagnostic criteria. Seventy-nine% of headaches were episodic and 21% chronic. Median time from first headache to initial hemorrhage was 1.5 years (interquartile ratio 0–3). Median hours between headache onset and SEHP was 1 in epistaxis, 21 in ecchymosis, and 0.5 in hematohidrosis. Twenty-four% had recurrent episodes of hemorrhagic phenomena.

Conclusion: Our results suggest that SEHP are features of PHDs. Future studies would benefit from systematic characterization of these phenomena in relation to headaches.

PO411

Headache pathophysiology and imaging

Diffusion tensor imaging analysis for patients suffering from migraine using tract-based spatial statistics

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The diagnosis of migraine is still generally made based on clinical symptoms, because there is no reliable diagnostic

test or imaging modality available. We therefore performed diffusion tensor imaging (DTI) for patients withmigraine and compared the findings with those obtained from normal volunteers. The diagnosis of migraine was made using the international classification of headache disorder. DTI was acquired using a 1.5 Tesla clinical magneticresonance imaging machine. A total of 89 migraine patients and 46 normal volunteers were examined by DTI, all in the same manner. The migraine patientswere divided into 2 groups according to their clinical outcome. The goodoutcome group included 61 patients with a good control of migraine after onemonth of medication. The poor outcome group included 28 patients with poorcontrol. There was no difference in age, sex, duration, frequency of migraine, presence of aura, or medication overuse headache. A whole-brain tract-basedspatial statistics analysis of DTI revealed the migraine patients with a goodoutcome to show a significantly lower fractional anisotropy (FA) at the corpuscallosum and on optic radiation. There was no difference between the FA of thepatients with poor control and normal volunteers. Our results demonstrated that DTI may be a useful diagnostic imaging modality for the patients with migraine and DTI could possibly predict the prognosis of migraine. FA changes might be the cause of migraine, and not the result of migraine, because the migraine duration and frequency were not related with FA.

PO412

Headache pathophysiology and imaging

Are subcutaneous triptans effective both early and late in the migraine attack? A mini-review

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Background: In a pivotal study Burstein et al observedthat 93% of nonallodynic attacks vs. 15% of allodynic attacks responded tosubc. sumatriptan. In contrast, Linde et al. found no difference between subc.sumatriptan given early or late (mean difference 5.7 h). Both studies were, however, open studies.

Aim: To find evidence for the efficacy of early orlate therapy with triptans in the literature.

Methods: Search for papers on RCTs with subc. triptans, published or from GSK Register.

Results:

Table 1. Headache response 1 h after subc. sumatriptan 6 mg in 2 randomised, controlled trials.

Time to administration	<4 h (n = 101)	>4 h (n = 318)
NEJM 1991	75%	71%
	0 h (n = 90)	4 h (n = 90)
GSK Register	72%	81%

Table 2. An example of very effective late treatment: Pain-free 2 h after subc. naratriptan

Dahlöf et al. Eur J Neurol 1998	Pain-free at 2 h	
	5 mg (n > 4 h = 23/34)	10 mg (n > 4 h = 20/34)
	79%	88%

Conclusion: Subcutaneous sumatriptan seems tobe equally effective when used early or late. Subcutaneous naratriptan (5 and10 mg) is very effective when used relatively late suggesting that a parenteraltriptan can overcome the problem with the allodynia likely present at this time.

PO413

Headache pathophysiology and imaging

Temporomandibular joint disfunction in migraine: mechanisms of comorbidity

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Temporomandibular joint disfunction (TMD) has been described in many studies, but detailed research of this condition in migraine is lacking. We analyzed the prevalence and clinical forms of TMD in migraine to study possible mechanisms of comorbidity.

Methods: We recruited 103 patients with migraine as defined by ICHD 3rd edition: 71 patients with chronic migraine (CM) and 32 patients with episodic migraine (EM). TMD was diagnosed using Research Diagnostic Criteria (RDC/TMD), anxiety was evaluated using the Hospital Anxiety and Depression Scale.

Results: Prevalence of TMD in migraine patients was 41.7%. In patients with rare EM (<4 migraine days/month) prevalence of TMD was 26.1%, while in the frequent EM (5–14 migraine days/month) plus CM group it reached 46.2% (p = 0.03).

Myofascial TMD was the most prevalent type in both groups. In patients with frequent EM or CM myofascial TMD comprised 63.8%, and Group II TMD – 34.1%. We found no association between the level of anxiety and presence of TMD.

Conclusion: TMD is highly prevalent in patients with migraine. Group I TMD, i.e. muscular dysfunction without joint involvement, was the most prevalent. We assume that central sensitization and dysfunction of antinociceptive systems play an important role in the pathogenesis of TMD in chronic migraine.

PO414

Headache pathophysiology and imaging

Vessel diameter measurements at the rat medullary brainstem in vivo

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Background: Neuronal activity can be quantified by direct and indirect methods, in the spinal trigeminal system electrophysiological recordings or post-hoc analysis via immediate early genes were previously used. Another option is coupling of blood flow to neuronal activity, also utilized in functional magnetic resonance imaging.

Aim: Clarify whether a continuous measurement of arterial vessel diameter in a dorsal view onto the medullary brainstem, utilizing neuro-vascular coupling, might serve as an indirect index of activity in the trigeminal brainstem.

Method: In anaesthetized rats, the medulla and the cranial dura mater were exposed. Activity within the trigeminal system was evoked by electrical stimulation. With a standard CCD camera and a further developed plugin for ImageJ to measure the vessel diameter, automated processing allows an evaluation immediately after acquisition.

Results: Keeping a clear view and compensation for the large ventilation and heart-rate associated movement were solved first. Then, electrical stimulation of the dura mater or the facial skin caused arterial vasodilatation. Repeated stimulation elicited similar responses. Evoked arterial vasodilation was eliminated after infusion of the CGRP receptor antagonist olcegepant.

Conclusion: CGRP released at the central terminals of activated trigeminal afferents has previously been shown to control the activity of central trigeminal neurons acting as a co-transmitter of glutamate. In our study an inhibition of vasodilation by olcegepant could be explained by inhibition of neuronal activity or CGRP spillover onto vascular targets.

PO415

Headache pathophysiology and imaging

Different cellular processes of pain reduction in head ache with LLLT

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Different cellular processes of Pain reduction in head ache with LLLT

Zarghi A [1]*

Low level laser therapy (LLLT) as a kind of treatment method in head ache for many years. This method has great potential for reducing pain, inflammation. Vast studies have been done in relation to different mechanisms resulting in photobiomodulation and pain reduction. After laser interaction with cells, different processes occur. Serotonin level (5-HT) will increase. Serotonin is a chemical messenger that transmits nerve signals between nerve cells. It also increases the Beta Endorphins, which reduces pain sensation. These increases can cause pain reduction in receptor site. Nitric oxide is crucial for natural potential action for impulse transmission in nerve cells that was enhanced after laser stimulation. It also has an effect on vasodilatation that increases oxygenation. Bradykinin becomes more in damaged tissues and causes pain sensation with stimulation of nociceptive afferents. Studies showed that laser therapy will help pain reduction by decreasing this peptide. Laser therapy also showed the following positive effects**:** Normalization of Ion Channels, Ca++, Na++, K+ proven to reduce pain levels. Blocked Depolarization of C-Fiber afferent nerves. Therapeutic lasers can suppress the excitation of these fibers, especially in low velocity neural pathways from nociceptors. Cellular studies help us better comprehension of mechanisms of laser therapy. The results of these studies are needed to be accompanied with clinical studies which have measurable outcomes. The studies showed promising results of the treatments.

Keywords: cellular processes, Pain, head ache, LLLT

PO416

Headache pathophysiology and imaging

Metabotropic glutamate receptor 5 antagonism reduces trigeminovascular nociceptive transmission

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Metabotropic glutamate receptors (mGluRs) modulate inflammatory and neuropathic pain, but have not been evaluated for their role in headache.

To establish the role of mGluR5 in an animal model of cephalic pain.

Trigeminovascular activation in rats as measured by arterial vasodilation after electrical stimulation of dura mater or by extracellular recordings in the trigeminal nucleus caudalis (TNC) has successfully predicted anti-migraine efficacy of DHE, triptans, and CGRP receptor antagonists. (Animal studies approved by IACUC and followed NIH guidelines.)

ADX10059, an mGluR5 antagonist, reduces neurogenic vasodilation at a dose of 20 mg/kg by $19 \pm 5\%$ ($F_{(5,25)} = 2.68$, $p = 0.045$). In contrast, inhibition of the NMDA receptor by MK-801 does not alter vessel dilation in response to dural stimulation ($F_{(1.4,8.5)} = 1.19$, $p = 0.331$). In support of these intravital microscopy data, evoked activity recorded from the TNC of anesthetized animals is significantly reduced by $24 \pm 6\%$ compared to pre-treatment baseline ($F_{(2.1,16.8)} = 4.63$, $p = 0.024$). Additionally, spontaneous activity of TNC neurons is reduced by $49 \pm 8\%$ ($F_{(1.89,15.0)} = 6.94$, $p = 0.008$). While overall activity in the TNC is blocked, sensory transmission in response to innocuous or noxious stimulation of the face is preserved. MGluR5 receptors are found in TNC neurons, suggesting a direct mechanism of action in the caudal brainstem.

These data support the use of mGluR5 antagonists as potential migraine therapeutics. The effect of ADX10059 on TNC spontaneous activity may also predict a role for mGluR5 inhibition as a migraine prevention strategy.

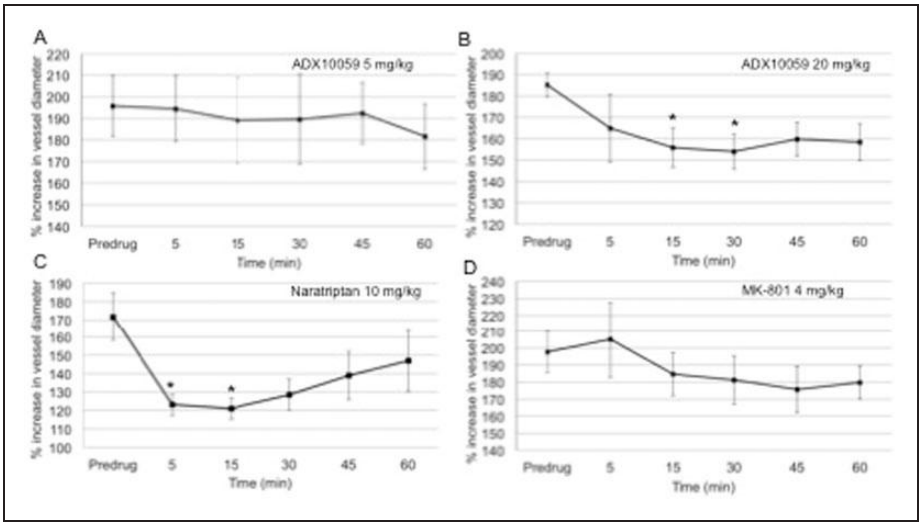

Figure 1. Intravital nicroscopy experiments demonstrating effects of serotonergic and glutamatergic agents on neurogenic dural vasodilation. Following control responses to electrical stimulation, rats were injected intravenously with the mGluRS inhibitor ADX10059 (A.B). natrip(an (C), or MK-801 (0) and electrical stimulation repeated after 5. 10. 15. 30. 45 and 60 minutes. $p < 0.025$, significance compared to control response.

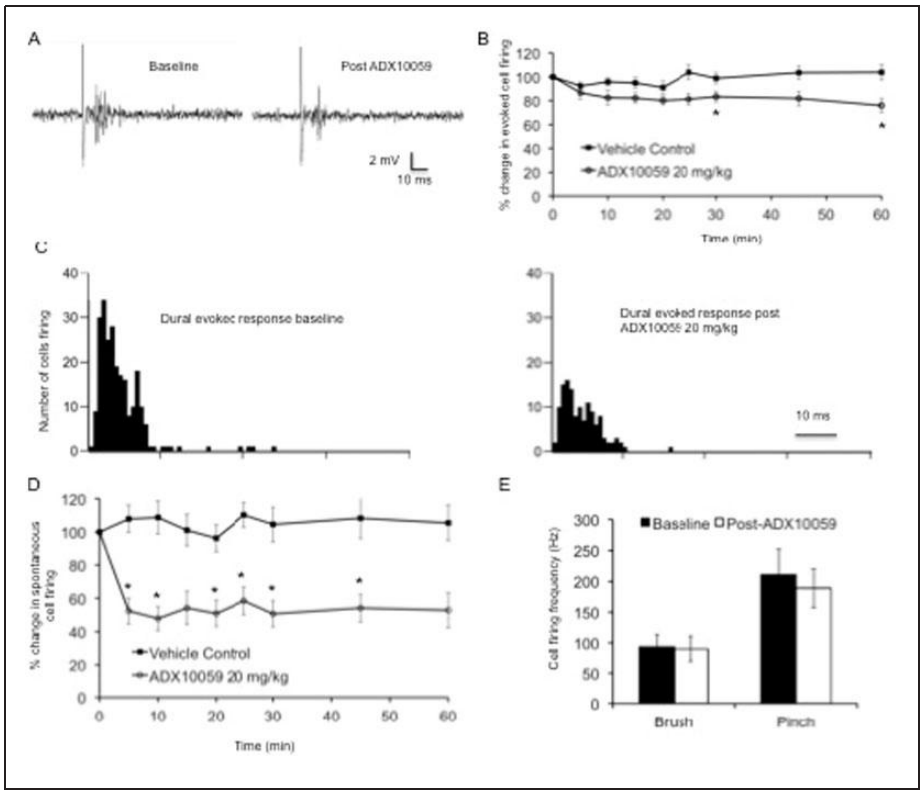

Figure 2. Single unit extracellular recordings in live, anesthetized Sprague Dawley rats A, Original tracing from a dural-evoked A Simbel fiber neuronal response before and after ADX 10059 (20 mg/kg). B. Time course summary of stimulus evoked responses in the presence of vehicle control (water or normal saline) and ADX10059 (20 mg/kg) C. Sample post-sbmi.dus histogram (cumulative over 20 evoked responses) identifying A Simbel fibers inhibited by ADX10059 D, Time course summary of spontaneous cell fining in the presence of vehicle control or ADX10059 E, Cell firing responses to light brush or noxious pinch over the VI dermatome. Data are presented as mean ± SEM: *p < 0.0167 in B. and *p < 0.008 in D when comparing to average of three baselines, using Student's paired t-test.

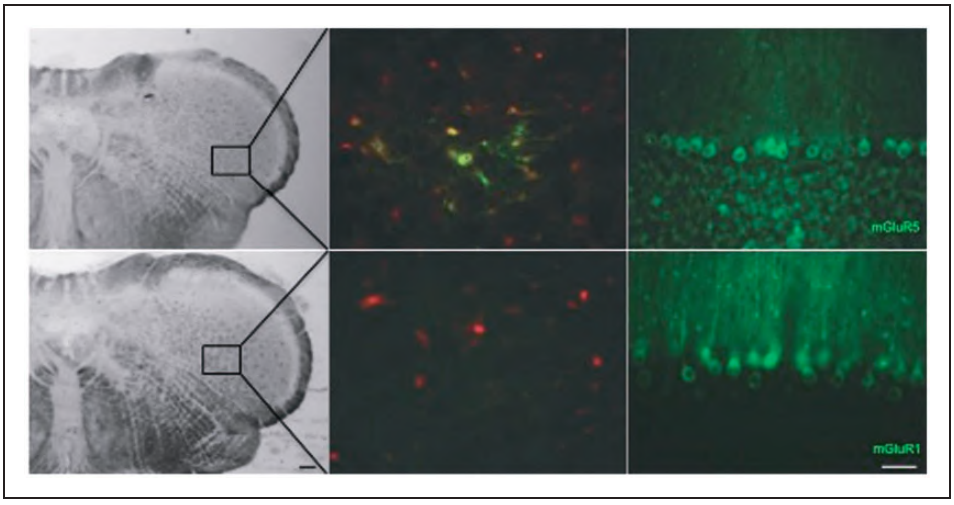

Figure 3. Immunohistofluorescent staining of group I mGluRs in naïve Sprague Dawley rats after intracardial perfusion with 4% paraformaldehyde.
A, B, Light photomicrographs of medullary brain slices containing the Sp5C nudeus at 25X magnification. Immunostaining for C, mGluRS *(green)* and D, mGluRl *(green)* co-labeled with NeuN (red) at 200X magnifiction Immunos1ing forE, mGluR5 and F, mGluR1 in the pyramidal layer of the carebelum at 200X magnification Scale bars = 200 μm (black). 50 pm (white)

PO417

Headache pathophysiology and imaging

Differences of central facilitation of trigeminal nociception between episodic and chronic migraine: nociceptive blink reflex and pain-related evoked potential study

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Introduction: The trigeminal nociceptive system plays a pivotal role in the pathophysiology of migraine.

Objectives: To investigate whether difference of trigeminal pain processing at brainstem as well as supraspinal level using nociceptive blink reflex (nBR) and pain-related evoked potentials(PREP) between episodic and chronic migraine (EM and CM, respectively)

Methods: 40 female patients with migraine (14 CM, 26 EM) according to the International Classification of Headache Disorders-3 beta version as well as 30 age-matched controls, were investigated using simultaneous recordings of the nBR and PREP during inter-ictal period.

Results: EM patients displayed significantly decreased latency, larger amplitude and AUC values of the R2 component in nBR, whereas decreased N2, P2 latency and larger N2-P2 amplitude in PREP compared with those displayed by controls ($p < 0.05$). But, CM patients displayed significantly smaller amplitude and AUC values of the contralateral R2 component in nBR, whereas decreased both P2 latency compared with controls ($p < 0.05$). Moreover, the amplitude and AUC of the R2 component in nBR was negatively correlated with the frequency of headaches in the migraineurs ($p < 0.05$).

Conclusions: Increased excitability of both trigeminal nociceptive processing on nBR and PREP was detected in patients with EM, but not of nBR in CM. EM patients show changes of nBR and PREP prompting to brainstem and supraspinal central facilitation changes of pain processing during interictal phases. R2 suppression at brainstem level associated with CM may be due to excessive supraspinal descending inhibitory influences.

PO418

Headache pathophysiology and imaging

Hand somatosensory sub-cortical sources are hypoactive in migraine interictally: a functional source separation analysis

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Background: Recent morpho-functional evidences pointed out that abnormalities in the thalamus could play a major role in the expression of migraine neurophysiological and clinical correlates. Whether this phenomenon is primary or secondary to its functional disconnection from the brainstem remains to be determined.

Aim: We used a Functional Source Separation algorithm of EEG signal to extract the activity of the different neuronal pools recruited at different latencies along the somatosensory pathway in interictal migraine without aura (MO) patients.

Method: Twenty MO patients and 20 healthy volunteers (HV) underwent EEG recording. Four ad-hoc functional constraints, two sub-cortical (FS14 at brainstem and FS16 at thalamic level) and two cortical (FS20 radial and FS22 tangential parietal sources), were used to extract the activity of successive stages of somatosensory information processing in response to the separate left and right median nerve electric stimulation. A band-pass digital filter (450–750 Hz) was applied offline in order to extract high-frequency oscillatory (HFO) activity from the broad-band EEG signal.

Results: In both stimulated sides, significant reduced sub-cortical brainstem (FS14) and thalamic (FS16) HFO activations characterized MO patients when compared with HV. No difference emerged in the two cortical HFO activations between two groups.

Conclusion: Present results are the first neurophysiological evidence supporting the hypothesis that a functional disconnection of the thalamus from the subcortical monoaminergic system may underline the interictal cortical abnormal information processing in migraine. Further studies are needed to investigate the precise directional connectivity across the entire primary subcortical and cortical somatosensory pathway in interictal MO.

PO420

Headache pathophysiology and imaging

Quantitative histological examinations on the dural vessels of hypoxic and normoxic mice: investigation of vascular remodeling

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Introduction: To examine both migraine and pulmonary hypertension (PH) we developed a hypoxic mouse model. Under hypoxic conditions (four weeks at 10% O_2) mice develop typical symptoms of PH, characterized by an increased muscularization of arterial blood vessels in the lung. The vessel remodeling can be prevented by the chronic application of 5-HT_{2B} receptor antagonists. We found that hypoxic mice also develop increased sensitivity towards the 5-HT_2 receptor agonist *meta*-Chlorophenylpiperazine (mCPP). In contrast to the control group (normoxic mice kept at 20% O_2) at low doses of 1 μg/kg body weight, mCPP triggers plasma protein extravasation (PPE) in the dura mater in hypoxic mice. Dural PPE is a quantifiable indicator of migraine-like events in animal models.

Aims: The sensitization towards mCPP may coincide with structural remodeling processes in arterial blood vessels of the dura mater, possibly exhibiting similarities to vascular alterations in the lung. To investigate this histological comparative examinations between hypoxic and normoxic mice groups were performed.

Methods: To quantify eventual vascular modifications whole mounts of the dura mater were immunohistochemically stained against alpha smooth muscle actin. The length of arterioles with a certain diameter ($Ø \geq 20\,\mu m$ and $Ø \geq 17$) was then measured.

Results: With the chosen comparison parameters no difference between hypoxic and normoxic mice could be detected.

Conclusion: The results indicate that the vessel remodeling occurring in the dura mater is different than the one in the lung. The detection of an eventual hypoxica dependent vascular remodeling in the dura mater requires further examinations.

PO421

Headache pathophysiology and imaging

Vagus nerve stimulation inhibits cortical spreading depression

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Background: Vagus nerve stimulation (VNS) has been reported to improve migraine. Cortical spreading depression (CSD) is the electrophysiological event underlying migraine aura, and likely headache.

Aim: To investigate whether VNS improves migraine by reducing CSD susceptibility.

Method: Male adult rats were anesthetized with isoflurane and systemic physiology monitored. For direct VNS (*dVNS; n = 24*), we placed a loop electrode around the mid-cervical portion of the vagus nerve. Stimulation (0.5mA, 30 s train of 0.5 ms pulses at 20 Hz) was delivered every 5mins for 1.5 h. For noninvasive transcutaneous VNS *(nVNS; n = 24)*, we placed electrodes contacting the skin overlying the right vagus nerve. Two 2-min stimuli (1 ms pulse of 5 kHz sine waves repeated at 25 Hz) were delivered with a 5-min interval. Sham groups had identical surgery but did not receive stimulation in either paradigm. CSD susceptibility was assessed by measuring the electrical threshold to provoke CSD and the frequency of CSD during continuous topical KCl on both hemispheres sequentially. CSD testing started during *dVNS*, and 30 min after *nVNS*.

Results: Both *dVNS* and *nVNS* suppressed CSD susceptibility (Figures 1& 2). CSD frequency was reduced by 25–40%, and CSD threshold elevated by 2–3 fold compared with controls. The *nVNS* paradigm was more efficacious than the *dVNS* paradigm. CSD suppression developed

within 30 min after VNS, and unilateral stimulation had bilateral effects.

Conclusion: VNS elevates the electrical threshold for CSD induction and reduces the frequency of KCl-evoked CSDs as preemptive and acute abortive treatment that may explain its therapeutic effect in migraine.

Figure 1

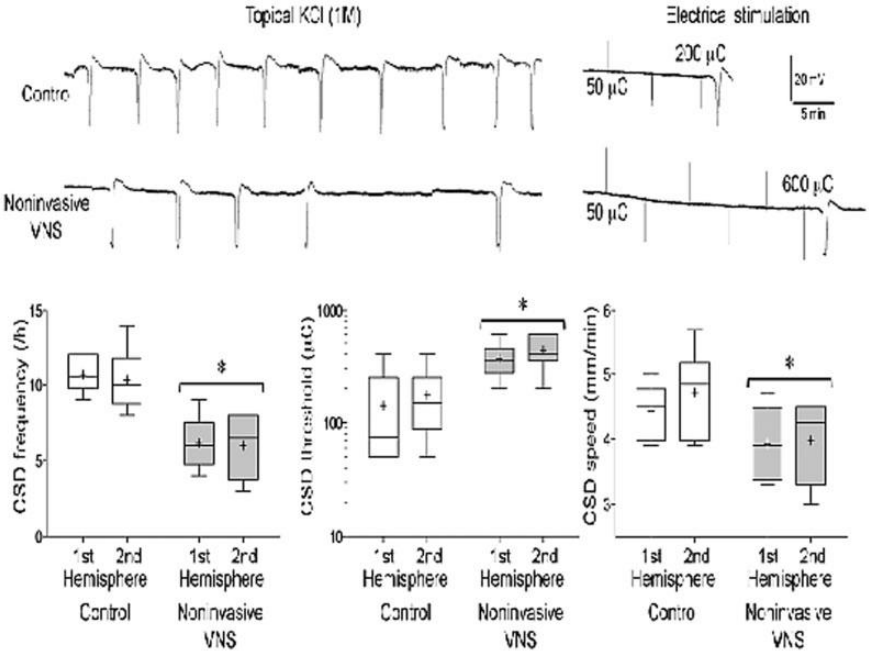
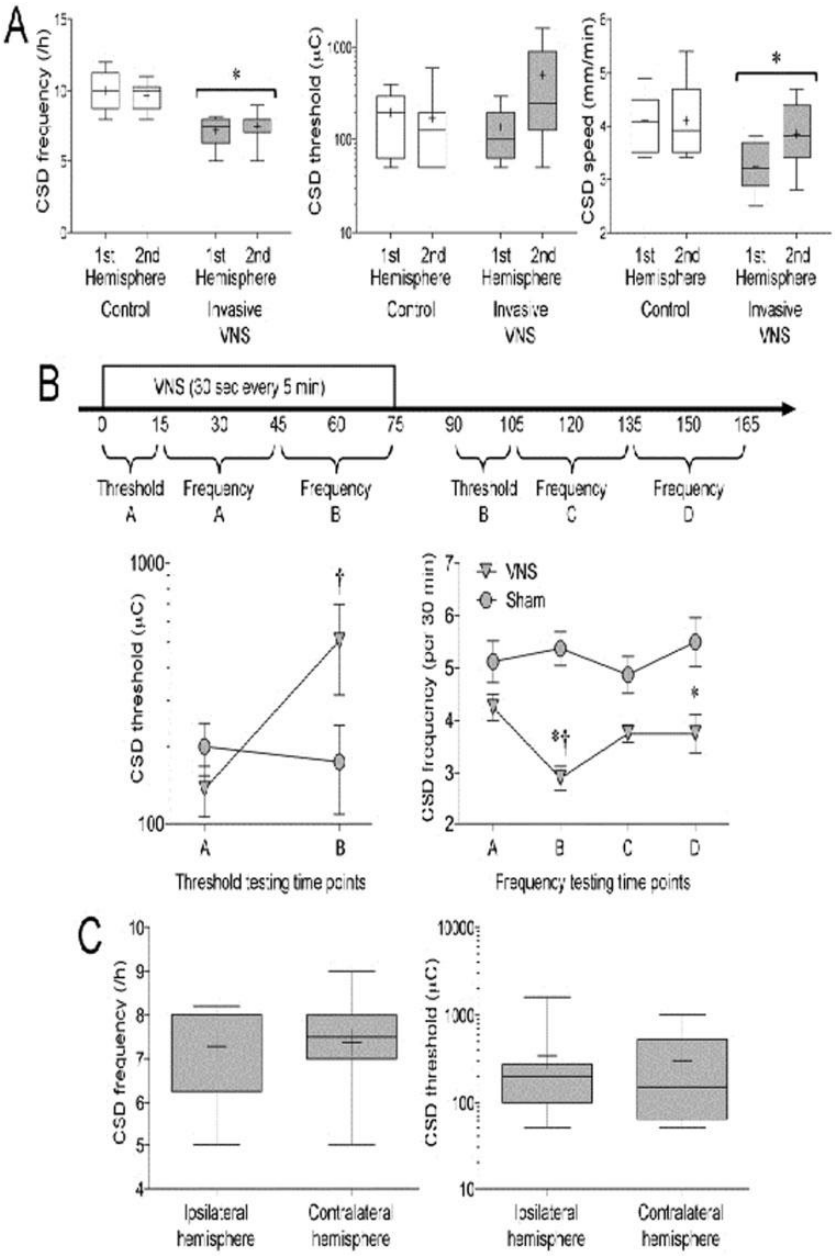


Figure 2



PO422

Headache pathophysiology and imaging

Modulatory role of endocannabinoids on gaba-a receptors of rat trigeminal sensory neurons

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Pharmacological activation of endocannabinoid CB1 receptors is proposed to control migraine headache via unclear mechanisms. We studied if trigeminal ganglion sensory neurons which express CB1 receptors contribute to this phenomenon. Whole-cell patch clamp recording from small-medium diameter sensory neurons of rat cultured trigeminal ganglia, tested anandamide (5 μM), an endogenous CB1 agonist, or AM251 (5 μM), a selective CB1 antagonist/inverse agonist, could modify neuronal excitability under voltage-clamp conditions at -65 mV holding potential. Neither anandamide nor AM251 had any effect on baseline current or conductance. However, anandamide strongly depressed the amplitude of GABA-mediated fast currents that were on average reduced by 85%. This

effect was manifested within 10 min and was reversible on wash. The depression by anandamide was unchanged in the presence of the TRPV1 antagonist capsazepine (10 μM), suggesting lack of involvement of TRPV1 channels. No effect was observed on P2X3 receptor-mediated currents. A different observation was obtained after 24 h application of anandamide, as GABA evoked fast currents remained similar to control. Application of AM251 for 24 h led to a large increase in GABA current amplitude (by 73%), a phenomenon subsequently inhibited by 10 min application of anandamide. These data suggest that GABA receptors were likely downregulated by constitutive CB1 activity (as demonstrated with AM251) and were further inhibited by acute activation of CB1 receptors. While ganglion GABA receptors are unlikely to modulate headache, our results indicate a mechanism whereby CB1 receptors could control migraine via GABA receptor inhibition in central pain networks. Supported by EuroHeadPain grant 602633.

PO423

Headache pathophysiology and imaging

Analysis of gene expression changes in a chronic migraine mouse model

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Background: Chronic migraine is characterized by the regular occurrence of acute pain attacks. The chronic nature of the disease and the underlying pathology are not understood. We developed a chronic migraine mouse model which enables the investigation of both acute and chronic aspects of migraine. The model is based on the assumption that the onset of a migraine attack is associated with the release of neuropeptides from the trigeminal nerve in the dura mater. We established that plasma protein extravasation as an indicative parameter for neurogenic inflammation in mice can be induced through 5-HT_{2B} receptor activation only after several weeks of hypoxia. Thus, we assume that hypoxia induces physiological adaptations which increase the sensitivity towards the induction of neurogenic inflammation in the dura mater.

Aim: The aim of this investigation is the identification of the hypoxia-induced physiological processes which lead to the previously described sensitization.

Methods: For this purpose mRNA expression profiles of the murine dura mater are generated.

Results: As a prerequisite for the further analysis a reliable protocol for the isolation and quantification of RNA from minute amounts of tissue such as the murine dura mater was established and optimized.

Conclusion: The identification of differential expression patterns is expected to provide insight into signaling pathways involved in the facilitation of the induction of PPE caused by hypoxia.

PO424

Headache pathophysiology and imaging

Examinations of mast cells in the dura mater in a migraine mouse model

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Background: The literature on migraine indicates the involvement of the serotonin 2B- receptor (5-HT_{2B}) and mast cells in the neurogenic inflammation of the dura mater. In this process the 5-HT_{2B} – receptor is hypothesized to induce a cascade of events which triggers vasodilation and the plasma protein extravasation (PPE) through mediators like calcitonin gene related peptide (CGRP) and substance P (SP). CGRP and SP can activate mast cell which release pro-inflammatory substances which trigger further inflammatory processes. This department is working with a chronic migraine model in mice. In this model, mice become sensitized by hypoxic treatment towards a migraine-related state in which the drug meta-Chlorophenylpiperazine (a partial 5-HT_{2B} agonist) can also induce a PPE. Little is known about the potential role of mast cell activation in these sensitization processes.

Aim: Here, we aim at investigating the role of mast cells in the sensitization process in the dura mater of mice.

Methods: The characterization of mast cells is done by immunohistochemical and histological stainings with different markers, e.g. FITC-Avidin.

Results: Mast cells in the dura mater of mice can readily be identified using common markers. Their spatial distribution is heterogeneous.

Conclusion: Murine dural mast cells exhibit some characteristics which are already described for other rodents like rats, but differ in other properties like distribution. This description allows further investigations of dural mast cells in mice.

PO425

Headache pathophysiology and imaging

Co-expression of the calcitonin receptor (CTR) and receptor activity-modifying protein (RAMP) 1 complex in the rat and human sensory trigeminal system

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Background: Calcitonin gene-related peptide (CGRP) has a key role in the pathophysiology of migraine and is associated with activation of the trigeminovascular system. Calcitonin receptor-like receptor (CLR) associates with receptor activity-modifying protein (RAMP) 1 to yield a functional receptor for CGRP. However, RAMP1 also associates with the calcitonin receptor (CTR), creating a receptor with high affinity for both CGRP and the related peptide amylin. The physiological significance and the distribution of both of these signalling units remains unclear but may be a potential avenue for refining drug design.

Aim: To study whether CTR/RAMP1 complex is expressed in relevant migraine related areas such as the trigeminal ganglion (TG) and spinal trigeminal nucleus (STN) in human and rat.

Method: Immunofluorescence was used to study the distribution and possible co-expression of RAMP1 and CTR in rat and post-mortem human tissue. Double-staining of CLR and CTR was performed in rat TG.

Results and Conclusion: In the TG expression of CLR, RAMP1 and CTR was detected. A subpopulation of RAMP1 positive TG neurons co-expressed CTR. No co-expression was observed between CLR and CTR. In the brainstem, we observed CTR expression in multiple regions, including the STN. Specifically, CTR was found in the fibers of sp5 and around fiber bundles in Sp5C. RAMP1-positive fibers were mostly observed in sp5. Co-expression of CTR and RAMP1 was detected in the fibers of sp5. Interestingly, blood vessels also co-stained for CTR and RAMP1. This study demonstrates the presence of CTR/RAMP1 complex at sites important for pain perception.

PO426

Headache pathophysiology and imaging

Kynurenic acid attenuates complete freund's adjuvant induced inflammation in the trigeminal ganglion

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Background: The trigeminal system has a pivotal role in the cranio-cervical pain process. Application of complete Freund's adjuvant (CFA) into the temporomandibular joint (TMJ) is a well-established model for activation of the trigeminal ganglion (TG). Kynurenic acid (KYNA) is an endogenous NMDA receptor blocker, which may have an anti-inflammatory effect.

Aim: Our goal was to investigate the time-related changes of the cell signaling pathways in the TG following *in vivo* application of CFA into the TMJ. We hypothesize that KYNA and its derivative kynurenic acid amide 2 (KYNAA2) might inhibit intracellular signaling pathways during CFA-induced activation.

Method: The TMJ inflammation was induced by CFA in rats. KYNA and KYNAA2 were intraperitoneal administered. We examined the mitogen-activated protein kinases (MAPKs as ERK1/2, p38 and SAPK/JNK), NF-κB, CaMKII and DREAM in the TG with immunohistochemistry and Western blot at 2 and 10 days post-CFA injection.

Results: The pERK1/2 and pp38 activations were seen in the satellite glial cells at 2 and 10 days post-CFA. Increased expression of CaMKII, NF-κB and DREAM were found in the neurons. Western blot confirmed the increase of pERK1/2 and pp38 in the TG. The elevated pERK1/2 protein level was decreased after KYNA, and the pp38 protein level was reduced after KYNA and KYNAA2.

Conclusion: The time-related changes of pERK1/2, pp38 and NF-κB in the TG point a possible neuron-glial interaction during this inflammatory process. The inhibition of MAPKs and NF-κB by the endogenous NMDA-receptor

antagonists suggests a crucial role of the glutamate receptors in the inflammation mechanism.

PO427

Headache pathophysiology and imaging

Thermal pain thresholds in migraine: comparison between episodic or chronic migraine patients and healthy volunteers using QST

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Background: Cutaneous allodynia is frequent interictally in migraine, more so in chronic (CM) than in episodic migraine (EM) (Schwedt et al 2011). In this study we assessed thermal pain thresholds with quantitative sensory testing (QST) in healthy volunteers (HV) and episodic (EM) or chronic migraineurs (CM) between attacks.

Subjects and Methods –Cold and heat sensory (CST & HST) and pain thresholds (CPT & HPT) were measured in 28 HV, 21 EM and 18 CM patients between attacks with a Medoc° Thermal Sensory Analyser. During incrementing or decrementing caloric stimulation with a 5.7 cm^2 probe placed on the forearm or the forehead subjects were asked to press a button when the stimulus was perceived and when it became painful. The means of 3 stimulations were compared between groups with One-Way ANOVA.

Results: There were no significant differences in forehead QST between the 3 groups. By contrast, in the forearm CST was increased in CM (28.35°C) compared to HV (29.72°C) ($p = 0.02$; $F = 3.73$), while HST was decreased (CM = 35.27°C; HV = 34.13°C) ($p = 0.004$; $F = 5.93$) and CPT decreased (CM = 19.12°C; HV = 12.69°C) ($p = 0.02$; $F = 3.93$). QST was not different between EM and HV.

Conclusions: Decreased forearm cold pain thresholds suggest that chronic migraine patients have selective extracephalic cold allodynia between attacks. Since forehead thermonociceptive thresholds are normal, this is probably not a consequence of the headache. Whether it might be explained by malfunctioning endogenous pain control or eventually involvement of the cold/menthol sensing TRPM8 receptor, of which the gene is associated with migraine in GWAS, deserves further research.

PO428

Headache pathophysiology and imaging

Modulation of the nociceptive blink reflex by repetitive transcranial magnetic stimulation in healthy volunteers: comparison of visual or motor cortex stimulation

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Background: Connexions between cortex and the trigeminal system may play a role in migraine. Repetitive transcranial magnetic stimulation (rTMS) of visual (Sava et al., 2014) or motor cortex (M1) (De Vito et al. 2009) modulates the trigeminal nociceptive system. In this study we searched which of visual or motor cortex rTMS has the greatest effect.

Subjects and Methods –Nociception specific blink reflexes (nBR) were recorded in 37 healthy volunteers (HV). rTMS of visual cortex was performed in 22 HV, M1 rTMS in 15 HV. With a figure-of-eight coil 800 pulses were delivered at 1 Hz or 10 Hz in random order on separate days. Before and after rTMS we measured sensory and pain thresholds, R2 area under the curve (AUC) and habituation on 15 averagings partitioned in 3 blocks of 5 responses.

Results: 1 Hz rTMS over visual cortex decreased pain threshold ($p = 0.001$), increased R2 AUC of the 1st nBR block bilaterally ($p = 0.02$) and increased habituation contralaterally ($p = 0.0002$). 10 Hz rTMS over the visual cortex had no effect on nBR.

Over M1, 1 and 10 Hz rTMS increased habituation contralaterally ($p = 0.004$ and $p = 0.01$ respectively), but had no effect on pain thresholds or nBR amplitude.

Conclusions: Visual rTMS is more effective on trigeminal nociception than M1 rTMS. In HV the visual cortex seems to have stronger functional connexions with the trigeminal nociceptive system than the motor cortex, which my have implications for the use of rTMS to treat trigeminal pain.

PO429

Headache pathophysiology and imaging

Migraine and gastric pathologies. A clinical study on 300 patients

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Background: The relationship between food consumption and migraine during migraine attacks has been widely reported by the literature. The predominance of gastrointestinal symptoms such as nausea, vomiting, diarrhea, etc. underlines involvement of the gastroenteric apparatus in migraine.

Aim: Our study is finalized to evaluate the clinical alterations of digestive apparatus in migraineurs.

Method: The research was conducted on 300 patients (224 women) with mean age of 36.9 (SD 15.8) years, suffering of migraine with and without aura (IHS '04 criteria). During the first visit, a detailed clinical computerized schedule was adopted involving all data with special regard to clinical signs of nutrients deficiency related to erratic food habits.

Results: Data obtained showed: altered breath 39,3%(118 pz); dry mouth 53,6%(161 pz); inflammation of the oral cavity 38%(114 pz); nausea 59,3%(178 pz); vomiting 47%(141 pz); pyrosis 56,3%(169 pz); slow digestion 55,3%(166 pz); gastralgia 61,6%(185 pz); meteorism 56,6%(170 pz); constipation 62,6%(188 pz); cold feet 44,3%(133 pz); limb cyanosis 16%(48 pz); cold hands 26%(78 pz); cramps 46%(138 pz); paraesthaesias at the upper and lower limbs 41,6%–43,6%(125 pz; 131 pz); diarrhea 60,3%(181 pz); unpleasant odor of faeces 47,3%(142 pz); photophobia 76%(228 pz); nyctalopia 47,6%(143 pz).

Conclusion: By analyzing the results, it has been evidenced in migraine the predominance of functional and organic gastric affections first of all gastritis. The gastric mucous impairment damaged the intrinsic factor production and reduced the activation of B12 vitamin and its coenzyme and their important functions. These data stress the role of gastroenteric dysfunction in migraine.

PO430

Headache pathophysiology and imaging

Serotonin depletion and plasticity of trigeminovascular system

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Background: Decrease in serotonergic neurotransmission plays an important role in pathogenesis of primary headaches. This reflects the effect of serotonin depletion on the trigeminovascular system.

Aim: To demonstrate the changes in neural and vascular components of the trigeminovascular system.

Method: Low serotonin state was induced in Wistar rats by administration of para-chlorophenyl-alanine. Anatomical and functional changes in serotonin depleted rats were investigated. Outcome measures included generation of cortical spreading depression, vascular responses, ultrastructural changes in cerebral endothelial cell, protein expression in trigeminal ganglia, trigeminal nucleus caudalis and cerebral microvessels.

Results: Depletion of serotonin caused substantial change in neural and vascular components of trigeminovascular system. The neural changes included an increase in cortical spreading depression generation, enhancement of trigeminal nociception, up-regulation of nNOS, CGRP and TRPV1 expression in trigeminal ganglia and increased phosphorylation of NMDA receptor in trigeminal nucleus caudalis. In the vascular compartment, low serotonin resulted in an enhancement of cerebral vascular response to vasodilating agents, increased microvascular endothelial pinocytosis and up-regulation of ICAM-1 and VCAM-1 expression in cerebral microvessels. We also found that the cerebrovascular changes observed in low serotonin animals could be reduced by inhibiting nitric oxide synthesis.

Conclusion: Our study demonstrates the response of trigeminovascular system to low serotonin condition. These plastic changes result in an enhancement of cortical excitability, facilitation of trigeminal nociception and increased vascular reactivity. Our results also suggest the pathophysiologic mechanisms underlying these changes may involve the activation of nitric oxide production.

PO431

Headache pathophysiology and imaging

Unbalanced plasma cytokine profile in women with episodic migraine: the "dark side" of the mood

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Background: Mounting evidence has linked increased pro-inflammatory and decreased anti-inflammatory cytokines with mood- and pain-related disorders, including Migraine (M).

Aims: To compare plasma cytokine profile between episodic M and healthy women and explore correlational data between plasma cytokines and mood.

Methods: We assessed anxiety (GAD7), Mood (POMS) and plasma levels of TNF-α, IL-1β, IL-6, IL-8, IL-10, and IL-12p70 (Flow cytometry) interictally in episodic M patients with/without aura (ICHD-II), taking no preventive medicine, from an outpatient clinic, and in heathy individuals recruited from local community.

Results: Thirty seven participants (age $= 34 \pm 10$, BMI $= 26.5 \pm 4.9$) were assessed (Control, n $= 17$; Migraine, n $= 20$). Groups matched on age, BMI, and aerobic fitness (VO2Max). M patients showed higher scores than controls on GAD7($p = 0.046$) and POMS-Tension ($p = 0.018$), and a trend of higher Fatigue-POMS($p = 0.08$). TNF-α($p = 0.009$) and IL-12p70($p = 0.01$) were increased, while IL-6($p < 0.000$), IL-8($p < 0.000$), and IL-10($p < 0.000$) were decreased in M patients. TNF-α and IL-12p70 were negatively correlated with IL-10 ($r = -0.795$ and $r = -0.826$, respectively, both $p < 0.0000$), while IL-10 positively correlated with IL-6 ($r = 0.874$, $p < 0.0000$) and IL-8($r = 0.725$, $p < 0.0000$). Multiple regression analysis models to test cytokine, BMI, age, and VO2Max as predictors of GAD7, Tension, and Fatigue showed that TNF-a (adjusted-$R^2 = 0.124$, i.e, 12.4% of variance in GAD7 explained by TNF-a), IL-8 (9.4%), IL-10 (20.6%), and IL-12p70 (38.5%) were predictors of GAD7. TNF-a (8.2%), IL-6 (11.8%), IL-8 (12.6%), and IL-12p70(25.5%) were predictors of Tension, and VO2Max (16.1%) and IL-12p70 (11.8%) predictors of Fatigue.

Conclusions: Unbalanced pro-inflammatory and anti-inflammatory plasma cytokine profile in M is coupled with increased anxiety and reduced mood.

PO434

Headache pathophysiology and imaging

Eicosapentaenoic acid/arachidonic acid ratio is associated with migraine chronification

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Background: The mechanism of migraine chronification is not yet fully understood but may involve in part increasing the frequency of migraine attacks. Cortical spreading depression (CSD) and neurogenic inflammation have been hypothesized to underlie pathophysiology of migraine attacks. Recent studies have reported that matrix metalloproteinase-9 (MMP-9) inducing an abnormality in the blood brain permeability, have been associated with CSD in migraine patients. Clinical treatment with eicosapentanoic acid (EPA), one of omega-3 polyunsaturated fatty acids has demonstrated to significantly reduce the activity of MMP-9.

Aim: To investigate the role of the EPA in migraine, we analyzed serum EPA/arachidonic acid (AA) ratio in migraineurs.

Methods: A total of 62 patients aged under 55 years, diagnosed with migraine (men/women, 10/52; mean age, 37.7 +/−10.5 years) and not taking medications containing EPA and AA were examined. Patients were classified the frequency of migraine attacks; 0–8 headache days per month, 9–14 headache days per month and 15- headache days per month. The level of significance was set at $p < 0.05$.

Results: The EPA/AA ratio in migraineurs was 0.202+/−0.117, mean+/−SD. The mean serum EPA/AA ratio significantly varied in proportion to the frequency of migraine attacks; 0.24 as 0–8 headache days per month, 0.19 as 9–14 headache days per month and 0.15 as 15- headache days per month. There was no significant difference between subjects having medication overuse or not.

Conclusions: Our results support the conclusion that reduced serum EPA/AA ratio is associated with migraine chronification.

PO435

Headache pathophysiology and imaging

Cortical thickness among headache sufferers in the general population (the MRI-HUNT study)

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Background: Several previous clinic-based case control MRI studies have found alterations in cortical thickness in a number of brain regions among headache sufferers. Many of these regions are involved in pain processing, suggesting a link between headache and brain morphology.

Aim: The aim was to investigate cortical thickness among headache sufferers and non-sufferers in a population-based study (MRI-HUNT) with a larger sample than previous clinic-based studies.

Methods: This study was part of a large longitudinal epidemiological study (Nord-Trøndelag Health Survey (HUNT)). The 1006 participants, 50–65 years at inclusion, had participated in all previous HUNT studies, and been randomly selected to a population-based imaging study of the head (MRI-HUNT, 2007–2009). The freesurfer software was used to determine cortical thickness in different areas of the brain. Headache sufferers were compared to headache-free in both cross-sectional and longitudinal ANOVA-analyses. In addition to an exploratory analysis, three a priori hypotheses based on previous studies were tested, postulating thinner cortex among headache sufferers in a) the prefrontal cortex (PFC), b) the anterior cingulate cortex (ACC), and c) the insula (all areas involved in pain processing).

Results: None of the a priori hypotheses were found to be true (PFC: $P = 0.644$, ACC: $P = 0.633$, insula: $P = 0.108$). Also, the exploratory analysis, using the predefined significance threshold ($P < 0.001$), showed no difference in cortical thickness between headache sufferers and headache-free.

Conclusion: The present large population-based study found no difference in cortical thickness among headache sufferers and headache-free implying that a history of headache may not influence brain morphology or vice versa.

PO436

Headache pathophysiology and imaging

Pilot study of neural correlates of chronic migraine: preliminary analysis of potential structural and functional changes

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Background: Migraine is a very debilitating, common and heterogeneous headache disorder with complex, but largely unknown pathogenic mechanisms. While the structural and functional neural correlates of episodic migraine (EM) are slowly being unravelled, less is known about its chronic form (CM).

Aim: The study's aim was to increase our understanding of the complex pathophysiology of CM by using a multimodal imaging approach during the migraine attack-free state.

Methods: Five female CM patients (39.4 ± 7.58 y; disease duration 23.8 ± 5.08 y) and 5 healthy sex-matched controls (28 ± 4.24 y) were examined. Functional neural correlates were assessed using 1) a seed-based BOLD resting state functional connectivity (RSFC) analysis, with the periaqueductal grey (PAG) and the hypothalamus as ROIs and 2) arterial spin labelling in an inter-ictal group perfusion analysis. Volumetric analysis in migraine-related subcortical structures and DTI were used to assess structural abnormalities.

Results: A number of regions involved in sensory and pain processing, particularly pain modulation (e.g. cingulate cortex and frontal lobes), were shown to have abnormal RSFC with the ROIs and increased perfusion during the inter-ictal period. Complementary structural connectivity was demonstrated with DTI in the region of the hypothalamus and the corona radiata.

Conclusion: This preliminary data provides evidence for EM and CM being a spectrum disorder with similar underlying pathophysiology. A dysfunction in both the regulation of the PAG (involved in anti-nociception/pain facilitation and sensory gating) and the hypothalamus (involved in endocrine responses and homeostasis) could play a central role in migraine pathophysiology, generating the migraine attack and causing premonitory symptoms respectively.

PO437

Headache pathophysiology and imaging

Long-term clinical and radiological follow-up in a sporadic hemiplegic migraine patient with the p. Ser218Leu CACNA1A mutation

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Background: Hemiplegic migraine patients with *CACNA1A* mutations often suffer from chronic progressive symptoms with an unclear prognosis.

Aim: To document the long-term clinical and radiological follow-up in a sporadic hemiplegic migraine (SHM) patient.

Methods: Clinical information was collected in a female SHM patient during outpatient visits and hospital admissions from age three to eighteen years. Cerebral MRI and MRS were performed repeatedly over the course of ten years.

Results: The SHM patient carries the p. Ser218Leu *CACNA1A* mutation and suffers from psychomotor retardation, with temporary deterioration of motor and cognitive skills after each attack. Apparent tonic-clonic seizures occurred during several attacks. Interictal examination at age eighteen revealed gaze-evoked nystagmus in all directions, mild ataxia in both arms and an ataxic gait, without paresis.

At age three, ictal MRI showed cortical swelling of the right hemisphere, with cortical diffusion restriction and pre-existent mild cerebellar atrophy. MRS showed a slightly lowered N-acetylaspartate/creatine ratio on the affected side. At age ten, cortical atrophy was observed in areas of previous diffusion restriction. At age twelve, ictal diffuse cortical swelling with diffusion restriction was seen in the left hemisphere. Interictal follow-up at age thirteen showed progressive cerebral and cerebellar atrophy.

Conclusion: This unique long-term follow-up of an SHM patient illustrates the occurrence of repeated cortical cytotoxic oedema and secondary progressive cerebral atrophy at a young age. Further studies have to show whether this partial transformation of areas with ictal diffusion restriction into cerebral atrophy might be prevented by aggressive prophylactic treatment in severe hemiplegic migraine.

PO438

Headache pathophysiology and imaging

Resting state functional connectivity abnormalities in pediatric patients with migraine

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Background: Previous resting state (RS) functional magnetic resonance imaging (fMRI) studies in adult migraine patients have demonstrated abnormal RS functional connectivity (FC) of brain networks involved in pain processing.

Aim: Aim of this study was to explore functional RS abnormalities in pediatric patients with migraine.

Methods: RS fMRI scans were acquired from 13 pediatric migraine patients and 15 age-matched controls. Independent component analysis and a template-matching procedure were used to identify the default mode (DMN), salience (SN), fronto-parietal attention (FPN), working memory (WMN), sensorimotor (SM), auditory and visual (VN) networks. Within-group and between-group RS FC comparisons and changes of interactions among RS networks were performed. Correlations between RS FC abnormalities and patients' clinical characteristics were also assessed.

Results: Compared to controls, pediatric migraine patients had an increased RS FC of the precuneus of the DMN and the dorsolateral prefrontal cortex of the right WMN. They also experienced a decreased RS FC of the anterior cingulum of the SN and the temporo-parietal junction of the left WMN. FNC analysis detected a decreased FC between the DMN and right WMN, and an increased FC between the VN and FPN in migraine patients compared to controls. No significant correlation was found between intra- and inter-network RS FC abnormalities and patients's clinical characteristics.

Conclusion: Significant RS FC abnormalities occur in pain-processing networks of pediatric migraine patients.

Brain regions involved in cognition were selectively involved, suggesting that abnormalities of cognitive modulation of pain in migraine patients occur from an early stage of the disease.

PO439

Headache pathophysiology and imaging

Structural cortical brain abnormalities in patients with vestibular migraine

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Background: Vestibular Migraine (VM) has been recently recognized as a migraine variant with vestibular manifestations. New advances in understanding the pathophysiology of VM have suggested a large overlap between migraine and vestibular pathways.

Aim: Aim of this study was to assess the regional distribution of gray matter (GM) abnormalities in patients with VM using voxel-based morphometry (VBM).

Methods: Using a 3.0 Tesla scanner, brain dual-echo and 3D T1-weighted scans were acquired from 20 patients with VM, 20 migraine patients with aura (MWA), 20 migraine patients without aura (MWoA) and 20 age-matched controls. VBM was performed using SPM8 and DARTEL. The correlations between regional volumetric abnormalities and clinical manifestations of the disease were also investigated.

Results: Compared to controls, all groups of migraine patients had GM atrophy of fronto-parietal regions and the cerebellum and an increased GM volume (GMV) of temporal areas. VM patients had a selective GMV increase of the left superior occipital gyrus, compared to controls and the other two groups of migraine patients. Increased GMV was detected in the right postcentral gyrus and left cerebellum in VM *vs*. MWoA. Compared to MWA, VM patients had an increased GMV of the red nucleus, left inferior temporal gyrus and right cerebellum. In VM patients, no correlation was found between GM abnormalities and patients's clinical characteristic.

Conclusion: Significant GMV abnormalities of multisensory vestibular cortical areas occur in VM patients. The distinctive increased volume of visual association areas in VM patients may be related to compensatory cortical plasticity of other sensory modalities.

PO440

Headache pathophysiology and imaging

Thalamo-cortical network changes during the migraine cycle: insights from MRI-based microstructural and functional resting-state network correlation analysis

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Background: Abnormal structural and functional plasticity in cortical and subcortical brain regions may be an important aspect of migraine pathophysiology. Resting state magnetic resonance imaging allows studying functionally interconnected brain networks. Whether there is a relation between the plasticity of resting state networks and integrity of thalamic microstructure during the migraine cycle is not known.

Aim: To verify functional connectivity between brain networks at rest and its relationship with thalamic microstructure in migraine without aura (MO) patients during and between attacks.

Method: Twenty-four patients with untreated MO underwent 3 T MRI scans during (n = 10) or between attacks (n = 14) and were compared to a group of 15 healthy

volunteers. We used MRI to collect resting state data among four selected resting state networks, identified using group independent component (IC) analysis. Fractional anisotropy (FA) values of bilateral thalami were retrieved from a previous diffusion tensor imaging study on the same group of subjects and correlated with resting state ICs Z-scores.

Results: We found a significant reduced functional connectivity between the default mode network and the visuo-spatial system between attacks, but between the executive control network and the dorso-ventral attention system during attacks. When HV and migraine groups were combined, ictal and interictal selected ICs Z-scores correlated negatively with bilateral thalami FA values.

Conclusion: The present results are the first evidence supporting the hypothesis that an abnormal dynamics of the connectivity between thalamus and functional cerebral networks at rest could contribute to recurrence of migraine attacks.

PO441

Headache pathophysiology and imaging

Increased tissue vulnerability to acute cerebral ischemic injury in migraineurs

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Background: Migraine, particularly with aura, is a risk factor for ischemic stroke. Recent data in migraine mutant mice suggest that cerebral hyperexcitability associated with migraine accelerates recruitment of ischemic penumbra into the core, resulting in faster infarct growth compared with wild type. We hypothesized that migraineurs are more likely to exhibit increased recruitment of ischemic tissue into the infarct in acute stroke.

Methods: We retrospectively identified subjects with reliably documented migraine history, measured lesion volumes on diffusion-weighted (DWI) and perfusion-weighted (PWI) MRI obtained within 72 h of symptom onset, and calculated the proportion of ischemic tissue on PWI hyperintense on DWI. Complete infarction pattern (i.e., no mismatch) was defined as PWI lesion $<120\%$ of DWI.

Results: Migraineurs ($n = 45$) were younger, more often female, less likely to have vascular risk factors, and more often had cervical artery dissection, but otherwise did not differ from controls ($n = 27$). A significantly larger proportion of migraineurs had complete infarction pattern, indicating that the entire perfusion defect was recruited into the infarct by the time of MRI (22% vs. 4% in migraineurs and controls, respectively; $p = 0.044$). The difference was even more prominent in migraineurs with aura (36% vs. 4%, $p = 0.019$). The association between migraine and complete infarction pattern persisted after adjustment for time to MRI ($p = 0.041$).

Conclusions: This case-control study shows that a history of migraine, particularly with aura, is associated with a complete infarction pattern during acute ischemic stroke, suggesting that a subset of migraineurs have an increased tissue vulnerability to acute cerebral ischemic injury.

PO442

Headache pathophysiology and imaging

The use of optogenetic stimulation for non-invasive induction of cortical spreading depression in anaesthetized and freely behaving mice

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Background: Cortical spreading depression (CSD), the correlate of migraine aura, is often induced by invasive stimulation. With optogenetics technology neurons expressing light-sensitive channelrhodopsin-2 ion-channels (ChR2) are depolarized by light. This can be used *in vivo* to activate cortical neurons in mice expressing ChR2 under control of the neuronal Thy1 promoter (Thy1-ChR2 mice).

Aim: Induce CSD non-invasively using transcranial illumination in anaesthetized and freely behaving Thy1-ChR2 mice.

Methods: Thy1-ChR2 mice were obtained from The Jackson Laboratory; for some experiments crossings were made with transgenic mice carrying familial hemiplegic migraine type-1 (FHM1) mutations. A 400μm optic fiber was placed on the skull overlaying visual cortex for light-activation while CSD recordings were obtained with glass (anaesthesia) or platinum (awake) electrodes in motor cortex with additional skull laser Doppler probes for non-invasive CSD detection. Blue light (470 nm) delivered at different intensities and durations was used for CSD threshold assessment and repetitive CSD-induction. Simultaneous video-recordings (awake) allowed behavioral analysis. Experiments were approved by the LUMC Animal Experiment Ethics Committee with care and handling according to the Dutch Law on animal experimentation.

Results: CSD induction with optogenetics was possible in anaesthetized and freely behaving Thy1-ChR2 mice. CSD was repeatedly inducible on one day (anaesthesia) and multiple days (awake). Pilots in double transgenics (Thy1-ChR2 and FHM1crossings) confirm their more severe CSD phenotype.

Conclusion: This study shows the potential of optogenetics for non-invasive CSD induction in anaesthetized and freely behaving mice and makes feasible detailed analysis of initiation mechanisms and impact of CSD related to migraine pathophysiology.

PO443

Headache pathophysiology and imaging

Inflammatory response in rat trigeminal ganglion induced by application of inflammatory agents on the dura mater

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Introduction: The trigeminal ganglion forms the converging point between the central nervous system and the peripheral structures such as cranial arteries, playing a crucial role in migraine pathophysiology.

Aim: We asked the question if local inflammation of the dura mater may induce inflammatory activation of the trigeminal ganglion.

Material and Methods: Inflammatory soup (IS), a mixture of agents involved in inflammation, or Complete Freund's Adjuvant (CFA) was administrated onto an exposed area of the rat dura mater *in vivo* and washed away with saline after 20 min. The cranial window was closed and animals were sacrificed 4 hours, 24 hours or 7 days after the operation. The trigeminal ganglia were removed and processed for immunohistochemistry or Western blot for protein quantitation. The study was approved by the Institutional Animal Care and Use Committee, the care and handling of the animals were in accord with National Institutes of Health guidelines for ethical animal treatment

Results: Both substances induced enhanced expression of pERK1/2, IL-1β and CGRP in the trigeminal ganglion. The pERK1/2 immunoreactivity was mainly observed in the satellite glial cells, while IL-1β positivity was present in the neuronal cytoplasm, close to the cell membrane, presumed as sign of neuro-glial interaction. Increased CGRP expression was observed in neurons and nerve fibres. Our Western Blot studies show the same tendency.

Conclusion: Our results suggest that application of inflammatory agents on the dura mater for causes long-term activation of the TG and support the role of neuro-glial interaction in activation of the trigeminovascular system.

PO444

Headache pathophysiology and imaging

Modulation of inflammatory mediators in the trigeminal Ganglion by botulinum neurotoxin type a: an organ culture study

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Background: The sensory innervation of the cranial structures originates primarily in the trigeminal ganglion (TG) with calcitonin gene-related peptide (CGRP) as the most expressed neuronal messenger molecule which is also released in migraine attacks. Onabotulinumtoxin type A (BoNT-A) has been found to reduce pain in chronic migraine.

Methods: Rat TGs were incubated for 24 hrs with either the CGRP receptor inhibitor telcagepant, the MEK1/2 inhibitor U0126, BoNT-A or NaCl, followed by immunohistochemistry with primary antibodies against CGRP, RAMP1 (CGRP receptor component), iNOS (inflammatory marker), SNAP-25 (synaptic vesicle docking protein), SV2-A (Botulinum toxin receptor element) or IL-1β.

Results: We found that the number of CGRP positive cells increased after U0126 and BoNT-A incubation. The granular cytoplasmic RAMP1 in fresh animals had in most cases disappeared in incubated groups. iNOS immunoreactivity was exclusively found in the SGCs in fresh, vehicle, U0126 and BoNT-A groups. Scattered cytoplasmic SNAP-25 immunoreactive granules were found in most neurons in fresh specimens. In the incubated groups, the staining had increased intensively. SV2-A immunoreactivity was confined to the SGC cytoplasm in all groups; no difference between the different incubation groups could be found. Almost all neurons in the fresh specimens displayed IL-1β immunoreactivity. The groups incubated with U0126 or BoNT-A showed none or little IL-1β immunoreactivity.

Discussion: We hypothesize that chronic migraine might be associated with some degree of inflammation in the TG that could involve expressional changes both in neurons and SGCs. The results of the present work illustrate one way by which BoNT-A may modify these expressional changes.

PO445

Headache pathophysiology and imaging

Modulate the nucleus raphe magnus increase cortical excitability and cortical blood flow

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Introduction: The nucleus raphe magnus (NRM) modulates pain transmission in the spinal cord through tonic inhibitory input from GABAergic neurons. The NRM is also known to modulate dural nociceptive processing in the trigeminocervical complex. However the modulation of the NRM on cortical activity and cortical blood flow (CBF) is still unclear.

Aims: To examine the effects of general inhibitor, lidocaine and GABA modulation in the nucleus raphe magnus (NRM) in cortical spreading depression (CSD) model.

Methods: Adult male Sprague-Dawley rats were anesthetized. We examined the effects of lidocaine and GABA microinjection into the NRM, on the depolarization shift (DC shift) and CBF. Saline of the same volume was given to the control animals. One hour after injection, CSD was induced by application of 3 mg of solid KCl on rat's parietal cortex. DC shift and CSD-evoked changes in CBF were recorded for one hour.

Results: Microinjection of lidocaine and GABA into the NRM increased the development of CSD and CBF. The number of DC shifts was 11 ± 2, 14 ± 2 and 13 ± 2 in the control and lidocaine and GABA groups, respectively. Similar pattern was observed in the peak hyperemia. The number of peak hyperemia was 11 ± 2, 15 ± 2 and 16 ± 2 in the control and lidocaine and GABA groups, respectively.

Conclusion: Our findings indicate that the inhibition of neurons by lidocaine and GABA in the NRM facilitates the cortical susceptibility as well as cortical blood flow. Demonstrating this modulation provides evidence for its dysfunction as a potential pathogenic mechanism in migraine.

PO446

Headache pathophysiology and imaging

Mrna expression profile of prostaglandin D2 receptors in rat trigeminovascular system, and effect of prostaglandins in rat migraine models

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Background: Prostaglandin D_2 (PGD_2) is a strong vasodilator of extracerebral arteries, but causes only mild headache in healthy volunteers.

Aims: 1.) To elucidate the mRNA expression profile of DP_1, DP_2 receptors and PGD_2 synthase (L-PGDS) in the trigeminovascular system (TVS); and other pain processing structures in rat brain; 2.) To study the effect of the DP_1 receptor antagonist, MK-0524, on PGD_2-induced vasodilation of middle meningeal artery (MMA) in rat closed cranial window (CCW) model; 3.) To investigate if an i.v. infusion of prostaglandin (PG) mix, PGD_2, PGE_2 and PGI_2 (iloprost), in awake rats activates nociceptive/neuronal activation markers in the TVS.

Methods: qPCR, the genuine rat CCW model, and the western blot technique were used to investigate the above mentioned aims.

Results: mRNA for DP_1, DP_2 and L-PGDS was expressed differentially in all examined tissues. The DP_1 receptor was highly expressed in trigeminal ganglion and dorsal root

ganglion. MK-0524 significantly (~62%, $p < 0.05$) blocked the PGD_2- induced dilation of MMA. No increase in p-ERK protein level was observed in the TVS after infusion of PG mix in awake rats. Neuronal activation markers, cFOS and EGR-1, were not changed in the trigeminal nucleus caudalis.

Conclusions: PGD_2 induced vasodilation of MMA is mainly mediated by activation of DP_1 receptors. Furthermore, high expression of DP_1 mRNA in TG and DRG suggest that PGD_2 might play a role in migraine pathophysiology. However, infusion of PG mix in awake rats did not activate nociceptive/neuronal markers in the TVS.

PO447

Headache pathophysiology and imaging

Towards a pragmatic migraine model for drug testing: 1. Cilostazol in normal subjects

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Background: A model for the testing of novel anti-migraine drugs should ideally use healthy volunteers for ease of recruiting. Cilostazol provokes headache in healthy volunteers with some migraine features such as pulsating pain quality and aggravation by physical activity. Therefore, this headache might respond to sumatriptan, a requirement for validation. The hypothesis of the present study was that sumatriptan but not placebo is effective in cilostazol-induced headache in healthy subjects.

Methods: In a double-blind randomized crossover design, 30 healthy volunteers of both sexes received cilostazol 200 mg on two separate days, each day followed by oral self-administered placebo or sumatriptan 50 mg. Headache response and accompanying symptoms were registered in a questionnaire by the participants themselves.

Results: Cilostazol induced a reproducible headache in 90% of the participants. The headache had several migraine-like features in most subjects. Median peak headache score was 2 on the sumatriptan day and 3 on the placebo day ($P = 0.17$). There was no reduction in headache intensity 2 h after sumatriptan ($P = 0.97$) and difference in AUC 0–4 h between two experimental days was not significant ($P = 0.18$). On the placebo day 8 participants took rescue medication compared to 3 on the sumatriptan day ($P = 0.13$).

Conclusion: Despite similarities with migraine headache, cilostazol induced headache in healthy volunteers does not respond to sumatriptan.

PO448

Headache pathophysiology and imaging

Refractory chronic daily headache and idiopathic intracranial hypertension without papilledema: preliminary results of an ongoing prospective study

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Background: A diagnosis of idiopathic intracranial hypertension without papilledema (IIHWOP) should be considered in unresponsive chronic daily headache (CDH) patients. Controversies exist regarding the CSF opening pressure (OP) cut-off value greater than 200 or 250 mmH2O and the role of transverse sinus stenosis (TSS).

Aim: To investigate the frequency of IIHWOP and TSS in adult patients with refractory CDH.

Methods: In a prospective study, patients with refractory CDH underwent ophthalmologic evaluation and Optical Coherence Tomography to rule out the presence of papilledema; cerebral MR venography (MRV) to detect TSS; and a lumbar puncture to measure OP. TSS was identified using a combined conduit score (CCS).

Results: Thirty-two patients were enrolled. Five patients were excluded due to protocol violations. Analyses were conducted in 27 patients (20 F, 7 M; mean age 51.2 ± 11.4; mean BMI 26.3 ± 5.3). None of the patients had papilledema. All displayed an OP lower than 250 mmH2O (range 102–245). Five (19%) had an OP greater than 200 mmH2O: three of them achieved an improvement of headache frequency or intensity after 12–18 ml CSF withdrawal. Fifteen patients (56%) had MRV evidence of TSS: bilateral in 4 and unilateral in 11. No significant correlation was found between CCS and OP.

Conclusions: In our series, all patients displayed normal OP values (<250 mmH20). Nineteen percent of patients had an OP greater than 200 mmH2O. However, we found

no correlation between transverse sinus stenosis and CSF opening pressure. A large number of patients is needed to confirm these preliminary findings.

PO449

Headache pathophysiology and imaging

Application of maldi mass spectrometry imaging for analysis of biomolecular profiles after experimental stroke in a migraine mouse model

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Background– **Matrix-assistedlaser desorption/ionization** (MALDI) mass spectrometry imaging (MSI)can identify biomolecules while maintaining spatiotemporal distribution intissue. Migraine is a risk factor for stroke but the underlying mechanisms areunknown. MSI after experimental stroke, induced by Middle Cerebral ArteryOcclusion (MCAO), in wild-type (WT) and familial hemiplegic migraine 1 (FHM1)mice can provide biomolecular profiles in the infarct core and penumbra and insightin molecular mechanisms relevant to migraine.

Aim: Implement MALDI-MSI for measuring biomolecularprofiles of FHM1 and WT mice after MCAO at specific brain regions to gaininsight in the biochemical processes involved in development of infarct coreand penumbra after stroke.

Method: 2–4months-old male FHM1 and WT mice were used. Twenty-four hours after MCAO micewere sacrificed using *in-situ* funnelfreezing or heat stabilization to prevent post mortem degradation. MALDI-MSI wasperformed on 12-μm coronal tissue sections for analysis of peptides, proteinsand metabolites. MSI datasets were co-registered to the Allen Brain Atlas tocompare the molecular signatures of distinct brain regions. Experiments wereapproved by the LUMC Animal Experiment Ethics Committee according to the DutchLaw on animal experimentation.

Results We wereable to apply MALDI-MSI for analysis of the distribution patterns of metabolites, peptides and proteins in brains of FHM1 and WT mice following MCAO.

Conclusion: MALDI-MSIcombined with experimental stroke in our migraine mouse model provides anunbiased approach to gain insight in the biomolecular pathways underlying therole of the penumbra in infarct size development in relation to migraine..

PO451

Headache pathophysiology and imaging

Increased susceptibility to hypoxic/ischemic injury in FHM1 mutant mice

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Background: Migraine, particularly with aura, is associated with increased risk of stroke both during and between attacks. Mechanisms are unknown. We recently showed that migraine mutations that enhance susceptibility to spreading depression render the brain more susceptible to focal ischemic injury by facilitating ischemic depolarization events akin to spreading depression.

Aim: To test whether migraine mutations sensitize the brain to hypoxic or global ischemic injury in vivo and in vitro.

Methods: Familial hemiplegic migraine type 1 (FHM1) homozygous S218L mutant mice and wild-type littermates were studied. For hypoxia, mice were placed in a chamber flushed with 7% O_2 (2 L/min) maintained at 27°C under normal atmospheric pressure, for a maximum of 6 hours or until they developed neurological signs. Global ischemia was induced by bilateral common carotid artery occlusion (BCCAO) under Isoflurane anesthesia for 20 min. Brain tissue was examined using H&E, fluoro-Jade B and c-Fos staining. Primary hippocampal cultures were subjected to oxygen/glucose deprivation (OGD) in vitro, high KCl or glutamate toxicity, and cell viability was measured.

Results: FHM1 mutant mice showed markedly increased incidence of seizures and early mortality during both hypoxia and BCCAO. Hippocampal injury was more

severe after BCCAO. OGD, high KCl or glutamate all caused significantly higher neuronal death in cultures obtained from FHM1 mutants compared with wild-type littermates.

Conclusion: These data suggest that genetic susceptibility to migraine and spreading depression increases sensitivity of brain tissue to hypoxic, global ischemic or excitotoxic insults as a fundamental mechanism to explain the migraine-stroke association.

PO452

Headache pathophysiology and imaging

Spreading depression-induced blood brain barrier disruption is prevented by RHO-Kinase inhibition and associated with increased transendothelial pinocytosis

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Background: The blood-brain barrier (BBB) is a dynamic structure that maintains brain homeostasis. Cerebral endothelial cells form the BBB by virtue of intercellular tight junctions, low expression of pumps, and low rates of transcellular pinocytosis. Spreading depression (SD) is the electrophysiological correlate of migraine aura and a trigger for headache.

Aim: Characterize BBB disruption following SD, and explore the underlying mechanisms in relation to rho-associated kinase (ROCK).

Methods: A total of six cortical SDs (CSDs) were evoked over 1 h by topical application of 300 mM KCl over the right hemisphere in anesthetized mice (male C57BL/6 J). BBB disruption was assessed by Evans Blue extravasation (EB, 2%, 3 ml/kg) in piriform cortices at 6 h, 12 h and 24 h after CSD. Endothelial cell ultrastructure was examined using electron microscopy 0– 24h after the same CSD protocol in order to assess vesicular trafficking. Mice were treated with vehicle, isoform non-selective ROCK inhibitor fasudil (10 mg/kg, IP 30 min), or ROCK2-selective inhibitor KD025 (200 mg/kg, PO bid for 5 doses).

Results: EB leakage was detectable within 6h, and increased over 24 h. Both fasudil and KD025 suppressed EB leakage without affecting CSDs. Pinocytosis was enhanced in the ipsilateral hemisphere at 6 h, reached a peak around 12 h, and returned to basal levels at 48 h. Other morphological indices of endothelial cells, including the thickness, length and transverse angle of tight junctions were unchanged.

Conclusion: These data demonstrate that SD-induced BBB disruption is prevented by ROCK inhibition, and suggest that transendothelial pinocytosis as the primary mechanism through which BBB is disrupted.

PO453

Headache pathophysiology and imaging

Neurophysiological aspects of ehlers-danlos hypermobility type patients affected by episodic migraine: a VEP/AEP study

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Background: Ehlers-Danlos Syndromes are a heterogeneous group of heritable connective tissue disorders characterized by joint hypermobility, skin hyperextensibility and tissue fragility. The hypermobility type (EDS-HT), is the most common and is associated with musculoskeletal pain, fatigue and headache. In particular, it is not clear whether migraine in these patients represents a secondary manifestation or an actual comorbidity.

Aim: In migraine, lack of habituation responses during repetitive stimulation is the most consistent interictal abnormality of cortical information processing observed. Aim of our study was to assess this neurophysiological aspect in EDS-HT patients affected by migraine, in order to evaluate if their brain responses differ from those of migraineurs or healthy subjects.

Method: Visual evoked potentials (VEPs) and Auditory Evoked Potentials (AEPs) were recorded in 15 EDS-HT patients affected by migraine without aura, 15 healthy volunteers (HV) and 15 migraine patients (MO).

Results: Preliminary results showed that by measuring the slope of the linear regression of VEPs, there was a significant lack of habituation in EDS-HT and MO patients respect to HV (0.53 and 0.5 vs. −0.02; $p = 0.009$ Figure 1). When measuring AEPs, we found lower initial amplitudes in EDS-HT respect to MOs and HV (15.16 vs. 18,76 vs. 21.25; $p = 0.04$) and we also confirmed a lack of

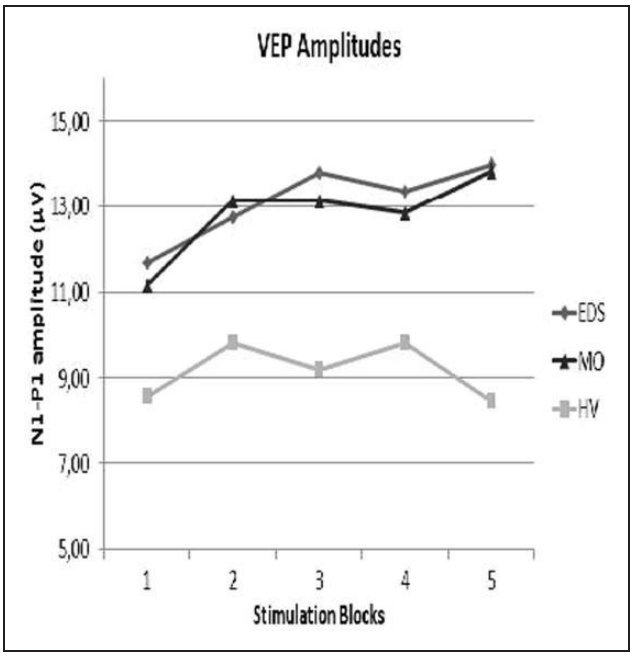

Figure 1. Slope of the linear trend of the N1-P1 VEP component

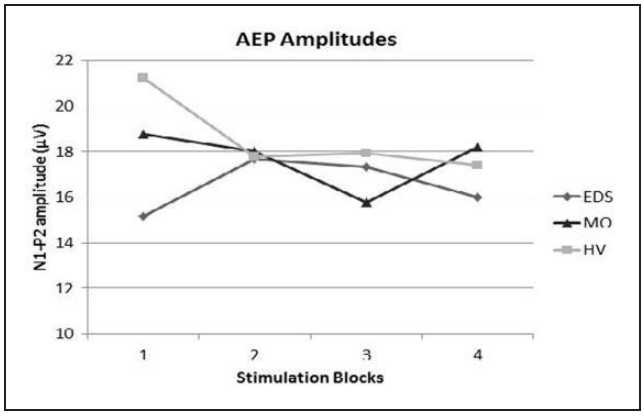

Figure 2. Slope of the linear trend of the N1-P2 AEP component

habituation respect to HV in both the MO and the EDS-HT group, which was significantly more evident for the latter ($p = 0.01$ Figure 2).

Conclusion: EDS-HT patients show the same neurophysiological abnormalities of migraineurs, suggesting that migraine in EDS represents a primary comorbid headache, rather than a secondary form.

PO454

Headache pathophysiology and imaging

Trigeminovascular activation and csd susceptibility in serotonin transporter gene knock-out mice: an attempt to disentangle the role of 5-HT neurotransmission and sex hormones in migraine

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Background: Migraine is a "low 5-HT" condition and sexually dimorphic. Several studies reported that serotonin transporter (5-HTT) gene polymorphisms might be involved in migraine susceptibility. Leao's cortical spreading depression (CSD) causes the migraine aura while the trigeminovascular system is responsible for the migraine headache and can be activated by nitroglycerin (NTG).

Aim: To study the CSD and NTG models of migraine in 5-HTT knock-out (KO) mice and search for gender differences.

Method: Both models were studied in male and female wild-type and 5-HTT KO mice. 1) CSD were elicited by applying over the occipital cortex a cotton ball soaked with 0.5 M KCl and recorded by DC electrocorticogram. 2) NTG (10 mg/kg) or its placebo were administered ip; 4 hours later animals were perfusion-fixed and cervical spinal cord was removed for immunohistochemistry.

Results: 1) In both sexes 5-HTT gene invalidation increased CSD frequency. This effect was more pronounced in KO females than in KO males, while wild-type animals did not differ. 2) The mutation had no influence on the NTG-induced increase of c-Fos immunoreactive neurons in the spinal trigeminal nucleus of females while this increase was attenuated in KO males.

Conclusion: 5-HTT gene invalidation increases CSD susceptibility more so in females, suggesting that decreased 5-HTT activity may aggravate migraine with aura. By contrast, it attenuates NO-induced trigeminovascular activation in males, which might predict a beneficial gender-specific effect on migraine headache. This illustrates the complex and differential relation between serotonergic transmission and sex hormones in both migraine types.

PO455

Headache pathophysiology and imaging

Regional cerebral blood flow changes in the early phase of provoked and spontaneous migraine attacks

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Background: Identification of brain areas that show functional changes during the earliest phases of a migraine attack will increase our understanding of where and how migraine starts and evolves.

Aim: To detect early migraine specific regional cerebral blood flow (rCBF) changes.

Methods: Fourteen female migraine without aura (MO) patients (age 24–51 years) and nine female controls (age 25–46 years) underwent three pseudo continuous arterial-spin-labeling perfusion-MRI scans. Glyceryl-trinitrate (GTN) was used to trigger MO attacks and controls underwent the same protocol. Measurements at baseline, and 90 minutes (GTN-90) and 270 minutes (GTN-270) after GTN infusion, corresponded with early migraine phases. Five migraineurs were scanned around the start of a spontaneous migraine attack.

Results: There were no differences in rCBF between migraineurs and controls at the subsequent timepoints after GTN-infusion. When analyzing migraineurs and controls as one group over-time, rCBF was significantly higher at GTN-90 in the right lateral occipital cortex, lingual gyrus, hippocampus, postcentral gyrus and precentral gyrus compared to baseline. At GTN-270 the rCBF increase in the right lateral occipital cortex persisted and a decreased rCBF in the thalamus and the posterior cingulate cortex was observed. During the spontaneous MO attack a modestly decreased rCBF in the thalamus was observed.

Conclusion: rCBF changes after GTN are probably not specific features of migraine pathophysiology. GTN-infusion by itself seems to result in brain-area specific rCBF changes that can persist for hours. Thalamic hypoperfusion could be a (non-specific) migraine trigger in susceptible persons.

PO456

Headache pathophysiology and imaging

Changes in nociceptive withdrawal reflex thresholds in women on oral contraceptive with migraine attacks in the suspension week

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Background: Migraine is a common and disablingneurological disorder that affects women three times more than men. Migraine isdeeply influenced by menstrual cycle and by estro-progestinic therapies.

Aim: The aim of this study was to investigate pain modulationeffect of estro-progestinic therapy in women with suspension-induced attacks.

Methods: We analyzed the nociceptive withdrawalreflex (NWR) obtained with electrical stimulation of the sural nerve. Reflexthreshold of NWR, considered as the lowest current intensity needed to evoke astable EMG response, was obtained with a single stimulus (RT-SS). Painintensity perceived at RT-SS was recorded by means of VAS. We enrolled 10 women(age 32.4 ± 8.6 years) affected by migraine without aura, with headache attacks-restricted to the suspension week of hormonal therapy. Patients underwent twotests: the first (T1) during the third week of estro-progestinic therapy, thesecond (T2) during the suspension week.

Results: At T1, RT-SS was 15.5 ± 6.8 mA (VAS 5.2 ± 2.1) with an average area under the EMG track of 1416.1 ± 711.1 mV/mS. At T2, RT-SS was 13.0 ± 5.6 mA (VAS 5.1 ± 1.9)with an EMG area of 1978.8 ± 1194.3 mV/mS. Statistical analysis showed that RT-SSwas significantly lower at T1 when compared with T2 values ($p < 0.005$). A tendency toward an increase was observed inthe EMG area, while no difference was observed as regards VAS rating of pain.

Conclusions: Suspension of estro-progestinic therapyis associated with a drop I neuro-physiologically recorded pain threshold.

PO457

Headache pathophysiology and imaging

Lack of habituation with nociceptive blink reflex in migraine

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Background: Migraineis related to abnormal central interpretation of normal sensory input in the trigemino-vascular system relaying via brainstem nuclei, whose functionality can be assessed by the habituation of the oligosynaptic nociceptive blink reflex. Previous research has suggested an interictal lack of habituation in migraine patients, although conflicting results have also been shown. Whether habituation changesprior to a migraine attack is unknown.

Methods: In a prospective case-control study, nociceptive blink reflex measurements were performed in n = 20 controls and n = 8 migraine patients. Different inter-stimulus-intervals (250 / 500 / 1000 / 1500 / 2000 ms) were used. Stimulationand recording were performed on ipsilateral and contralateral sides.

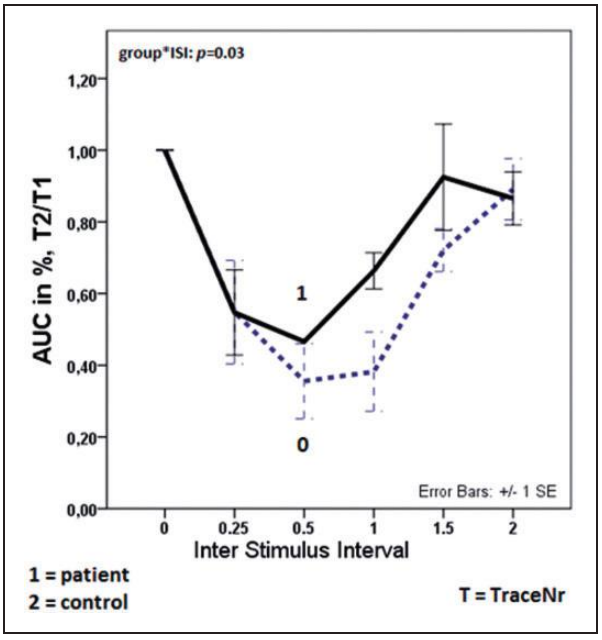

Figure 1. Response (habituation) to ipsilateral blink blink reflex in migraine patients is different to non-headache controls (p = 0.03)

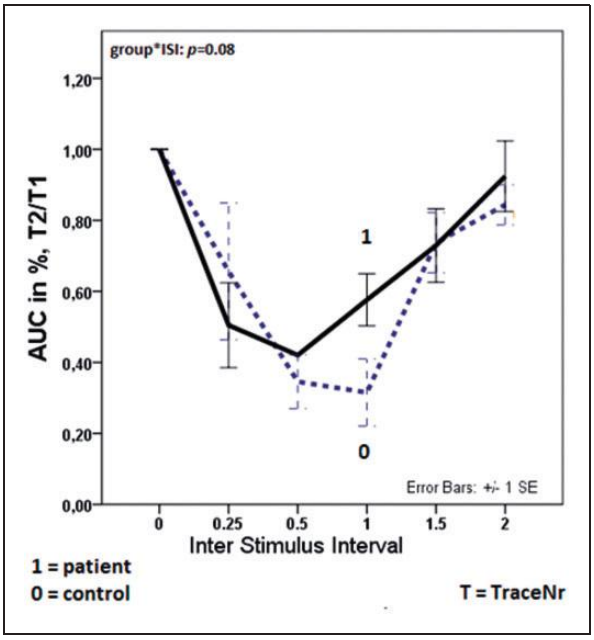

Figure 2. Response (habituation) to contralateral blink blink reflex in migraine patients and non-headache controls is not significantly different (p = 0.08)

Habituation was defined as Data were analysed by a generalized estimating equations model.

Results: At baseline, theresponse to the first stimulus did not differ between groups ($p > 0.05$). When measuring on theipsilateral side, interictal migraine patients showed less habituation compared to non-headache controls ($p = 0.03$; Fig1). Contralaterally, there was no significant difference ($p = 0.08$; Fig 2).

Conclusion: Migraine patients show interictal, ipsilateral decreased habituation of the blink reflexcompared to non-headache controls, suggesting a different activation state of the trigeminal nuclei.

PO458

Headache pathophysiology and imaging

Female migraine without aura patients are not associated with structural grey matter or microstructural white matter abnormalities

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Background Previous: MRI studies in migraineurs reported various areas with both grey matter and (micro)-structural white matter differences. However, most studies involved small study populations with intermixed migraine subtypes and severities. Further, results were often inconsistent, and validity of analysis-methods has been questioned. Results and their migraine-specificity remain therefore unsure, and the clinical relevance unknown.

Aim: To assess regional grey and white matter (micro)-structure with state-of-the-art MRI techniques, in female migraine without aura (MO) patients.

Methods: Using high-resolution whole brain 3.0T MRI we acquired 3DT1-weighted and diffusion tensor images (DTI, 32 gradient directions). Regional grey matter differences were assessed using the FSL VBM-pipeline in 43 MO patients and 33 matched controls (mean age: 37.2 ± 9.6 vs 35.3 ± 9.8). Differences in white matter microstructure were assessed with DTI indices (FA, MD, AD and RD) using the FSL TBSS- pipeline in a subset of 27 patients and 20 controls (mean age: 36.6 ± 9.8 vs 32.8 ± 10.1). General linear models controlling for age with a threshold-free cluster-enhancement and family-wise-error-correction were applied to assess differences.

Results There were no significant differences in (regional) grey matter volumes and (regional) DTI indices of the white matter between the study groups.

Conclusion: In this study, using proper methodology, we were unable to identify significant structural grey or white matter differences between female migraine without aura patients and matched controls.

PO459

Headache pathophysiology and imaging

Pain modulation is affected differently in medication-overuse headache and chronic myofascial pain – a multimodal MRI study

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Background: Medication overuse headache (MOH) is a chronic headache that develops during overuse of acute pain medication. Neuroimaging studies revealed structural and functional changes in MOH, but it remains unclear whether similar changes could be observed in other chronic pain disorders.

Methods: In the present study we investigated functional connectivity (FC) with resting state fMRI and white matter integrity with DTI in patients with MOH ($N = 12$) and in patients with chronic myofascial pain (MYO; $N = 11$) compared to controls (CN; $N = 17$).

Results: Using a data-driven approach, we found that hyperconnectivity within the saliency and inferior frontal networks are a feature of MOH but not of MYO, whereas hypoconnectivity in fronto-parietal attention network was found in both pain groups. In a seed-to-whole brain analysis (seed: periaqueductal grey), patients with MOH had lower FC in parieto-visual areas and higher FC to inferior- and orbito-frontal regions. In contrast, MYO had lower PAG-mediated FC to somatosensory cortex and temporal regions, and higher FC to the inferior frontal gyrus. Using DTI, we found increased FA in the right insula and decreased FA in right parietal operculum for both MOH and MYO compared to CN. In contrast, MOH had increased FA also in the left insula, left nucleus accumbens, supplementary motor area/middle cingulum, posterior cingulum compared to CN. In MOH a positive correlation between FA and headache frequency was found.

Conclusions: The saliency network is particularly involved in MOH, as evidenced by FC and WM alterations. Pain modulation systems are affected in distinct ways in MOH and MYO.

PO460

Headache pathophysiology and imaging

Structural brain alterations in chronic migraineurs – a voxel based morphometry study

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Background: Episodic migraine may evolve slowly to chronic migraine. Voxel based morphometry MRI studies in episodic migraine (EM) have demonstrated structural changes in regions involved in pain processing. Some of these changes correlated with migraine duration and attack frequency suggesting that migraine is a progressive disorder of the brain with proceeding structural alterations of the brain. To assess this concept we evaluated possible structural alterations of gray matter in patients with chronic migraine (CM) and EM compared to healthy controls

Methods: Gray matter (GM) volume of individually age- and gender-matched subjects with CM without aura, EM without aura and healthy controls ($n = 21$ per group) was compared using T1-weighted magnetic resonance imaging at 3 T and voxel based morphometry.

Results: We found GM volume increase in CM compared to healthy controls in amygdala, putamen, hippocampus and insula. Comparison of EM with healthy controls revealed mainly a gray matter decrease in frontal gyrus. Considering episodic and chronic migraineurs, headache frequency was positively correlated with gray matter alterations in the temporal and frontal gyrus, amygdala and putamen. Disease duration was mainly associated with gray matter increase in the insula.

Conclusion: Chronic migraine is associated with gray matter changes in regions involved in pain perception and processing but also in affective and cognitive aspects of pain. GM Alterations in CM did not resemble that of EM. Some structural alterations were correlated with disease severity and duration in both groups. These findings underline the assumption that chronic pain alters the plasticity in the central nervous system.

PO461

Headache pathophysiology and imaging

Functional hyperconnectivity in patients with migraine: a resting functional magnetic resonance image study

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Background: Electrophysiological studies demonstrated various sensory evoked potentials (i.e. somatosensory, visual, or auditory) are exaggerated in patients with migraine. The thalamus stands on the common pivot, and may therefore be the culprit of hyperexcitability. Whether the functional connection of thalamus to its downstream substrate is hyper-connected in patients with migraine remains undetermined.

Aim: To explore the resting state functional network of thalamus between patients with migraine and control subjects, by using resting functional magnetic resonance imaging (rf-MRI).

Method: Thirty patients with episodic migraine (8 male, aged 33.8 ± 9.8 [mean $\pm$ SD]) and 29 control subjects (8 male, aged 32.1 ± 8.3) were recruited. The average headache duration was 14.8 ± 10.8 year, and the average migraine frequency was 3.2 ± 2.7 attacks per month. All patients received rf-MRI during their interictal state (no headache occurred within 72 hours prior to or after the scan). Using rf-MRI, whole-brain functional connectivity maps were derived from seeds placed within bilateral ventral posteromedial nuclei (VPM) of thalamus.

Results: In patients with episodic migraine, the functional connectivity between right VPM and bilateral auditory cortices were higher than those in control subjects (uncorrected voxel-wise threshold $p < 0.005$, with clusters passing FDR corrected $p < 0.05$). The figure derived from left VPM showed a similar figure, however, the significance was not reached.

Conclusion: Our study showed the functional connectivity between VPMs and bilateral auditory cortices were hyper-connected. It may account for the clinical presentation of phonophobia in patient with migraine, even during interictal state.

PO462

Headache pathophysiology and imaging

Carotid agenesia, migraine and tension type headache an unusual association

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Introduction: Migraine is a disorder affecting between 10 and 20% of the general population. There is evidence of a possible comorbidity between migraine and several diseases; furthermore, according to its wide diffusion, there

is the possibility of the casual association between migraine and many intracranial diseases, as in the case here reported.

Case report A 19 year-old woman presented complaining a headache never previously reported, since about three months. The patient, otherwise healthy, suffered of migraine without aura. She has been presenting MO monthly principally menses related (ICHD-III criteria), since she was 15 year-old. MO attacks were characterized by pulsating, moderate or severe pain localized in right or left front-temporal region and generally spreading to ipsilateral side of the head, lasting about 6–12 hours. During the attacks she presented phono-photophobia, nausea and the pain was exacerbated by movements and efforts. Neurological and physical examinations, blood tests, electrocardiogram were normal. The attacks were well responsive to NSAID's and their frequency stable. The new headache had tension type features (ICHD-III) nevertheless considering recent appearance she performed brain MRI and angio-MRI that showed a complete agenesia of left common carotid.

Discussion: Common carotid artery (CCA) agenesis, is a well-described yet extremely rare congenital anomaly. Most carotid system anomalies are related to origins of the external or internal carotid arteries. In our case is difficult to relate headache with this vascular malformation. We believe the case of interesting for the never previously report of the CCA with migraine and tension type headache.

PO463

Headache pathophysiology and imaging

Pain matrix activation by sustained noxious-innocuous thermal stimuli transitions: A comparative fMRI study in episodic migraine, medication overuse headache and healthy volunteers.

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[2]*Dept. of Neurology and Psychiatry, La Sapienza University of Rome, Rome, Italy*
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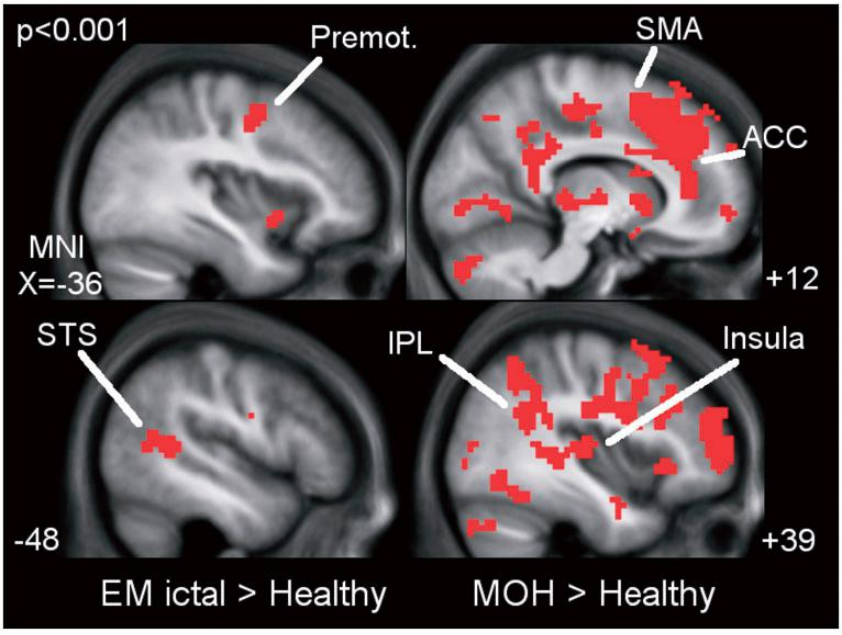
Background: The cerebral network termed the "pain matrix" includes areas such as anterior cingulate cortex, insula, SI, SII, medial temporal cortex and prefrontal cortex shown to respond to noxious stimuli, but also to other highly salient stimulations. We have previously shown in healthy volunteers that switching between noxious and innocuous sustained thermal stimuli induces a widespread nonspecific salience activation of the pain matrix (Bogdanov et al., 2015).



Aim: To assess if pain matrix areas are differently activated by salient transitions between sustained thermal stimulations in medication overuse headache and during migraine attacks.

Methods: We measured brain activation induced by sustained noxious-innocuous thermal stimuli transitions on the foot using fMRI in patients with episodic migraine (EM, n = 19, 5 during attack), medication overuse headache (MOH, n = 7) and in healthy volunteers (n = 24). The salience response in the pain matrix was significant (p = 0.05 FWE) in all subject groups. In MOH patients, the salience response was increased in the premotor cortex, superior temporal sulcus, supplementary motor area, posterior insula, anterior cingulate cortex and inferior parietal lobule, while in EM patients during attacks only activation in the premotor cortex and superior temporal sulcus was greater than in healthy controls.

Conclusion: This study shows hyperactivation of affective and cognitive cerebral areas in MOH patients and, to a lesser extent, in EM patients during migraine attacks.

PO464

Headache pathophysiology and imaging

Assessment of the excitability of the nociceptive blink reflex in headache attributed to temporomandibular disorders. Preliminary results

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Background: Altered sensory thresholds and excitability of nociceptive blink reflex (nBR) have been found in migraine and tension-type headache (TTH). In headache attributed to temporomandibular disorder (HTMD) nBR and thresholds have never been assessed.

Aim: To assess sensory thresholds and the excitability of the nBR in HTMD.

Method: 6 HTMD patients,fullfilling criteria established by the IHS in 2014, and 6 sex and age matched controls were studied. Electrical stimulii of 0,2msg were applied to the supraorbital nerve and sensory thresholds were calculated according to the method of limits. Pairs of stimulii were applied at 100, 200, 500, 750, 1000 and 1250 ms of interval (i.i) and at the pain threshold intensity. Area under curve of all recordings and the percentage of the response recovery was calculated. U Mann-Whitney test was employed to compare data.

Results: The mean of the perception and pain thresholds in patients and controls was 3,6 and 3,3mA and 5,1mA and 5,6mA respectively. No statistically significant difference was found ($p > 0,05$).

The recovery of the response at 100 ms i.i was 29%, 16,2% at 200 ms, 33% at 500 ms, 72% at 750 ms and 111,3% at 1250 ms i.i. In controls the recovery of the response was 34,6%, 45,3%, 69,5%, 32% and 66,7% respectively. Statistically significant difference was found at of 750 ms i.i ($p < 0,05$).

Conclusion: Sensory thresholds were not altered in HTMD.

Excitability of nBR is not impaired in HTMD. These preliminary data differ from previous results of altered excitability in other headaches such as TTH and migraine.

PO465

Headache pathophysiology and imaging

Systolic volume and cardiac output reduced in standing position in patients with chronic migraine

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Background and Aim: Neurovascular disorders are involved in the pathophysiology of migraine. Factors related to these disorders are not fully known. Changes in venous return may promote an increase in peripheral vascular resistance with consequent cerebral hypoperfusion transient followed by compensatory dilation of blood vessels induced by trigeminal vascular system. In investigate the disorders of the autonomic control and hemodynamic parameters in patients with chronic migraine.

Methods: Patients migraine n = 24 women (30 ± 9 years) and healthy control n = 12 women (31 ± 4 years) who underwent the examination of hemodynamic tilt test: peripheral vascular resistance index (PVRI); index stroke volume and cardiac output index; blood pressure (BP) and average heart rate (HR). For determination were performed tilt testing (tiltteste) to 70°. Patients were evaluated at three

periods: the supine position (S) in the first five minutes (5 ') and between 15 and 20 minutes (20') of inclination.

Results: There were no differences regarding BP and HR between the groups. There was a reduction in PVRI 5 'to 20' slope steeper in Migraine group (from 2597 to 2219) compared to the control (2137 to 1931); (* $p < 0.05$).

Conclusions: The group with migraine presented IS and IC lower than in the control group and greater reduction in PVRI 20'de slope, revealing a more pronounced reduction in venous return not adequately compensated by RVP in 20 minutes of tilt. Central sensitization of chronic migraine may be related to peripheral vascular disease.

PO466

Headache pathophysiology and imaging

Effect of acupuncture stimulation on cerebral blood flow using arterial spin labeling MRI in patients with migraine (2)

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Purpose: This study was tocontinue acupuncture treatment (acupuncture) in migraine for 4 weeks and toanalyze the change in cerebral blood flow (CBF) before and after acupuncturestimulation (stimulation) to examine the mechanism of action of acupuncture.

Method: The subjects were 10 women; 33.0 y.o. on average who satisfied the criteria for migraine accordingto the ICHD3β. Inserted bilaterally at temporal, masseter, splenius, trapezius muscle. The sites of stimulation included ofthe temporalis muscle, the masseter muscle, the upper trapezius muscle and thesplenius muscle. Stimulation was performedusing nonmagnetic silver needles (diameter: 0.2 mm, length:50 mm) for 10 minutes. 3TMRI and the pulsed ASL method were used to measure CBF. CBF wasmeasured between attacks 6 times, for 4 minutes each time; namely, before stimulation(pre), 5 minutes afterthe start of stimulation, 10 minutes after the start of stimulation, immediately after its completion, and 15 and 30 minutes after its completion. The CBF images obtained were statistically analyzed by SPM. The change by stimulation was compared between that before acupuncture and the pre-CBF after acupuncture.

Result: The pre-CBF of after acupuncture inboth temporal lobes compared with that at baseline but increased in the leftfrontal lobe and in the right occipital lobe. As for the change induced by stimulation, the CBF in the thalamus and insula after acupuncture was comparable with thatbefore acupuncture.

Conclusion: When acupuncture was conducted on migraine, there was a difference between the baseline pre-CBF andthat after 4-week. Moreover, the reactivity in the pain-related region also decreased.

PO467

Headache pathophysiology and imaging

Gabaa receptor alpha 2 subtype activation suppresses cortical spreading depression in chick retina

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Cortical spreading depression (CSD) is a transient propagating neuronal excitation followed by depression, which is generally accepted as the underlying cause of migraine. The inhibitory γ-aminobutyric acid type A ($GABA_A$) receptor activation was previously reported to reduce CSD frequency and propagation, but also relieve migraine headache. In this study, we further determined the role of major a subtypes of $GABA_A$ receptor in mediating CSD genesis and propagation using an efficient *in vitro* chick retinal model. We firstly demonstrated that abundant α2 and α5 of $GABA_A$ receptor expression in the chick retina, enabling the tissue useful for studying $GABA_A$ receptor pharmacology and SD. Marked suppression of CSD by SL651498 and TPA023 were observed at 10 μM and 50 μM respectively, suggesting a critical role of $GABA_A$ receptor α subtypes, in particular α2, in modulating retinal SD elicitation and propagation. The negative data on NS11394 at 3 μM and the little positive selectivity of TPA023 for α5 did not support that α5 subtype is involved in SD genesis and propagation. Our data provides strong evidence that α2, but not α5 is involved in early stage of migraine, indicating that α2 subtype a possible drug target related to migraine with aura.

PO468

Headache pathophysiology and imaging

Hyperechogenicity of the periaqueductal gray in migraine as a potential marker of progressive dysfunction: preliminary results

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Background: It is widely accepted that the brainstem plays a role in migraine pathophysiology. The periaqueductal gray matter (PAG) is a substantial component of the descending pain modulatory network. Previous MRI studies by Welch group demonstrated that PAG iron levels are abnormally high both in episodic and chronic migraine, suggesting the hypothesis that iron accumulation may be a marker of progressive PAG dysfunction. The increase in iron levels can be investigated with transcranial sonography (TCS) because of heavy metal-induced hyperechogenicity.

Aim: The purpose of our study is to evaluate hyperechogenicity of PAG in patients with episodic migraine (EM) and in subjects with chronic migraine associated with medication overuse headache (CM + MOH).

Method: So far, we have evaluated 8 patients diagnosed with EM and 8 patients with CM + MOH. TCS was performed using Acuson Sequoia ultrasound machine with a 2-MHz transducer. The sonographic parameters were set according to standard literature criteria.

Results: PAG echogenicity was higher in patients with CM + MOH than in those with EM: 6/8 CM + MOH patients (75%) showed PAG hyperechogenicity, while only 1/8 (12.5%) in the EM group.

Conclusions: These preliminary findings suggest the occurrence of a progressive degeneration of PAG in migraine. The possibility to reliably detect it with TCS would provide a low-cost, harmless, widely available tool. Evaluation on a larger population is needed to confirm PAG dysfunction in chronic migraine and the reliability of TCS for screening purpose and to predict the evolution of the disease.

PO469

Headache pathophysiology and imaging

Sleep quality and pain thresholds in subjects with tension type headache and migraine compared to healthy controls

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Background: Headache patients report more sleep disturbances than healthy controls. What is the relationship between subjective and objective sleep and pain sensitivity in migraine and tension-type headache?

Methods: A blinded, controlled, cross sectional study with polysomnography, measurements of pain thresholds (PT), data from headache and sleep diaries and questionnaires. We included 34 healthy controls, 50 migraineurs and 20 patients with TTH. Migraineurs who had their sleep recording more than 2 days from an attack were classified as interictal while those registered less than 2 days from an attack were classified as either preictal or postictal. Migraineurs with attack debut time mainly during night or by awakenings was classified as sleep migraine (SM). Migraineurs without a preference for nightly attacks were classified as non-sleep-migraine (NSM).

Results: Both TTH and NSM patients had more slow wave sleep (SWS), less fast arousals, more daytime tiredness and a tendency to lover PT than healthy controls; consistent with sleep deprivation. However, the sleep diary showed no difference in sleep time between headache patients and healthy controls. Migraineurs had shorter latency to sleep onset in the preictal phase than in the inter-ictal phase. SM patients had slightly increased number of awakenings than controls and less SWS than NSM.

Conclusions: Reduced arousal level and a tendency to reduced PT among TTH and NSM patients may be related to a *relative* sleep deprivation. Except for the SM group, our data indicate that subjects with headache may need more sleep than healthy controls.

PO470

Headache pathophysiology and imaging

Toll-like receptors: a new key in the pathophysiology of migraine

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Background: Molecular mechanisms related to migraine pathophysiology remain partially unknown. Activation of trigeminal neurons triggers an intense neuroinflammatory response that could be a consequence of Toll-like receptors (TLR) activation. However the clinical and therapeutic significance is not so clear.

Aim: To analyze the expression of TLR2 and 4 in neutrophils and monocytes of migraine patients and control subjects, together with the expression of endogenous ligands such as cellular fibronectin (cFn), in order to evaluate the role of TLRs in the pathophysiology of migraine.

Method: We performed a case-control study including 111 patients with migraine (39.7 ± 12.4 years; 93.7% women) (IHS 2013 criteria) and 20 control subjects (35.9 ± 8.8 years; 90.0% women). We analyzed epidemiologic, clinical and therapeutic variables. Mean expression of TLR2 and 4 on monocytes (TLR2M & TLR4M) and neutrophils (TLR2N & TLR4N) were analyzed in free-pain periods by flow cytometry. Serum levels of cFn were measured by ELISA at the same time that TLR2 and 4 expression.

Results: Patients with migraine showed higher expression levels of TLR4N (3839.9 ± 1167.4 vs.1804.4 ± 279.4 AFU (arbritary fluorescent units); $p = 0.001$); TLR4M (6265.3 ± 4404.1 vs. 2464.5 ± 640.9 AFU); TLR2N (839.3 ± 297.3 vs. 608.5 ± 177.6 AFU); TLR2M (1840.8 ± 880.4 vs. 731.3 ± 192.1 AFU) than control subjects (all $p < 0.0001$). We found a correlation between serum cFn levels (endogenous ligand of TLRs) and TLR4N ($r = 0.238$; $p = 0.007$); TLR4M ($p = 0.296$; $p = 0.001$); TLR2N ($r = 0.266$; $p = 0.003$); and TLR2M ($r = 0.348$; $p < 0.0001$).

Conclusion: Increased expression of TLR2 and 4 is found in migraine. These findings suggest that innate immunity is involved in migraine pathophysiology and that TLR2 and 4 expression may constitute a migraine biomarker.

PO471

Headache pathophysiology and imaging

Pentraxin-3 and stweak as key molecular markers of inflammation and endothelial dysfunction in migraine

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Background: Previous studies have suggested the role of endothelial dysfunction in migraine. Soluble TNF-like weak inducer of apoptosis (sTWEAK) and pentraxin 3 (PTX3) are determinants of endothelial dysfunction. We hypothesize that both sTWEAK and PTX3 act as biomarkers of endothelial dysfunction in migraine patients.

Aim: We aimed to study endothelial function with new biochemical (sTWEAK and PTX3) and ultrasonographic markers in patients with migraine.

Method: We performed a case-control study including 111 patients with migraine (39.7 ± 12.4 years; 93.7% women) (IHS 2013 criteria) and 20 control subjects (35.9 ± 8.8 years; 90.0% women). Clinical variables were recorded. We also analyzed flow-mediated dilation (FMD) in the dominant brachial artery. sTWEAK and PTX3 serum levels were measured by ELISA during interictal periods.

Results: Patients with migraine showed higher serum levels of sTWEAK (250.8 ± 212.8 vs. 23.5 ± 11.1 pg/mL) and PTX3 (1292.5 ± 518.9 vs. 486.3 ± 286.9 pg/mL) than control subjects (all $p < 0.0001$). No changes were found for FMD in migraine patients (18.2 ± 20.9 vs $15.1 \pm 11.3\%$; $p = 0.517$) compared to control subjects. However, we found a significant correlation between FMD and serum levels of sTWEAK ($r = 0.228$; $P = 0.009$) and PTX3 ($r = 0.193$; $p = 0.028$). Serum levels of sTWEAK and PTX3 increased with the time of evolution of migraine ($r = 0.199$ and $r = 0.213$, respectively) (all $p < 0.05$). Likewise, sTWEAK ($r = 0.450$) and PTX3 ($r = 0.349$) (all $p < 0.0001$) were significantly associated to the severity of attacks.

Conclusion: Patients with migraine showed increased levels of sTWEAK and PTX3. Furthermore, sTWEAK and PTX3 levels increase as migraine progresses in time. These findings suggest altered endothelial function in patients with migraine.

PO472

Headache pathophysiology and imaging

Brainstem infarcts and migraine headache

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Background: Imaging studies have shown a consistent activation of the brainstem during migraine attacks raisingthe question of its role in attack pathogenesis.

Aim: To determine the impact of brainstem lesions in migraine hypothesizing that it could change its course in differentways.

Methods: Consecutive patients withbrainstem stroke admitted to a rehabilitation center were asked about previous headache patterns and were enquired about the onset of new headaches following stroke. Brainstem stroke was diagnosed on the basis of clinical presentationand imaging exams and migraine according to the ID-Migrane.

Results: From a total of 46 patients with the diagnosis of brainstem stroke admitted during a period of 5 years, it was possible to interview 37. There 27 were women (73%) with a mean age of 57,1 years at the time of stroke and a mean follow up time since stroke onset of 4,6 years.

Only 8 (21,6%) individuals refer migrainein the past, of whom 7 reported disappearance of migraine headaches afterstroke. In the majority of these patients (56,8) the lesion was located in pons. Two patients described the onset of migraine like headaches *de novo* following stroke (6,9%).

Conclusion: Brainstem stroke isassociated to changes in migraine headaches during the period of 5 yearsfollowing stroke which suggests that the brainstem participates in the pathogenesis of migraine attacks. The exact location of brainstem lesion was not possible to specify in this series of patients and is necessary to understand in futurestudies.

PO473

Headache pathophysiology and imaging

Disrupted functional connectivity density of the brain in medication overuse headache using resting state fMRI

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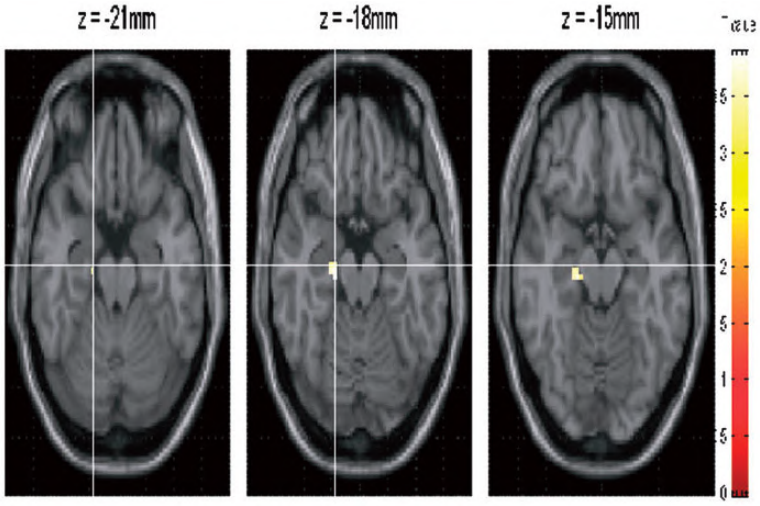
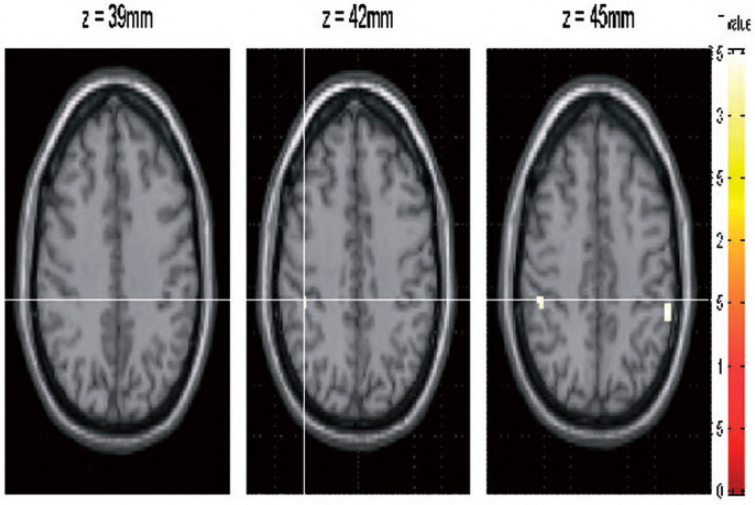
Purpose: To investigate the functional connectivity density (FCD) changes of the brain in the patients with medication overuse headache (MOH).

Materials and Methods: Conventional MRI, 3D structure images and resting-state functional MRI (rs-fMRI) were performed in 37 patients with MOH and 32 matched normal control subjects. Voxel-based whole-brain correlation analysis was performed to compute the whole-brain connectivity($r > 0.25$). Then, the sum of the weights of the significant connections was obtained for each voxel and considered as functional connectivity density. Finally, the individual FCD was converted into a z-score map and was analyzed using two sample *t*-test.

Results: Compared with normal controls, the decreased FCD over the whole brain was demonstrated in right





parahippocampal gyrus (MNI 21 -18 -18) (Figure 1), and the increased FCD located in left inferior parietal gyrus(MNI −54 −39 48) and right supramarginal gyrus (MNI 51 −33 48) (Figure 2).

Conclusion: These results suggest that MOH is associated with intrinsic functional connectivity density changes, and it may also have some common neurophysiologic features with addiction. And the further neuromechanism should be investigated.

PO474

Headache pathophysiology and imaging

Peripheral and cen2tral sensitization in patients undergoing occipital nerve stimulator insertion for intractable migraine

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Introduction: Central sensitization and impaired conditioned pain modulation (CPM) response has been reported to contribute to migraine progression (1). Migraine patients can present with allodynia possibly attributed to increased sensitivity of peripheral ends of nociceptors with both peripheral and central sensitization. Occipital nerve stimulation (ONS) works by stimulating the distal branches of C2 and C3 possibly altering the nociceptive traffic to the trigemino-cervical complex, brainstem and supranuclear connections.

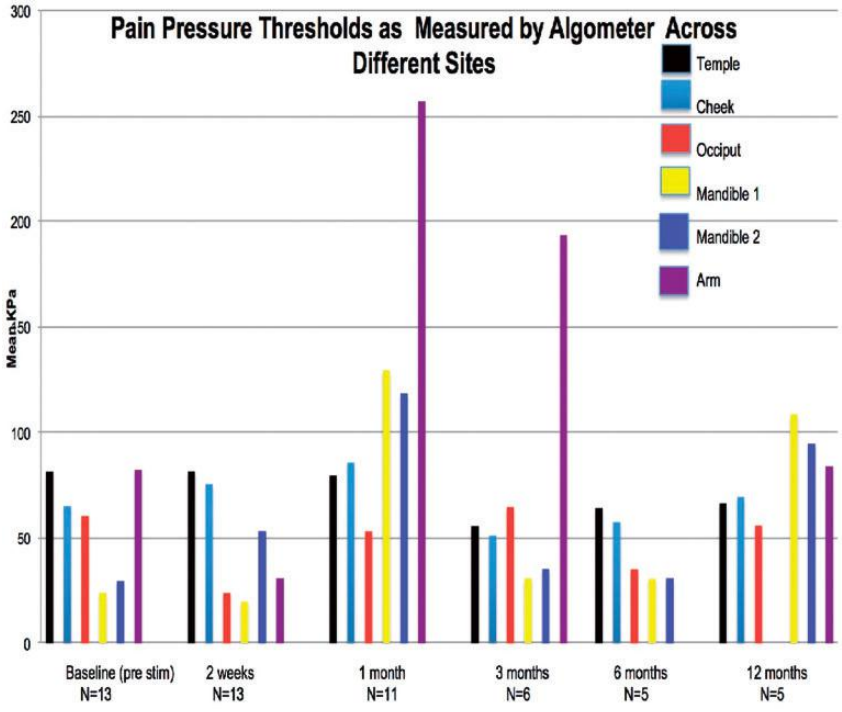
Aims: This observational study explores peripheral and central sensitization in patients undergoing ONS for intractable chronic migraine

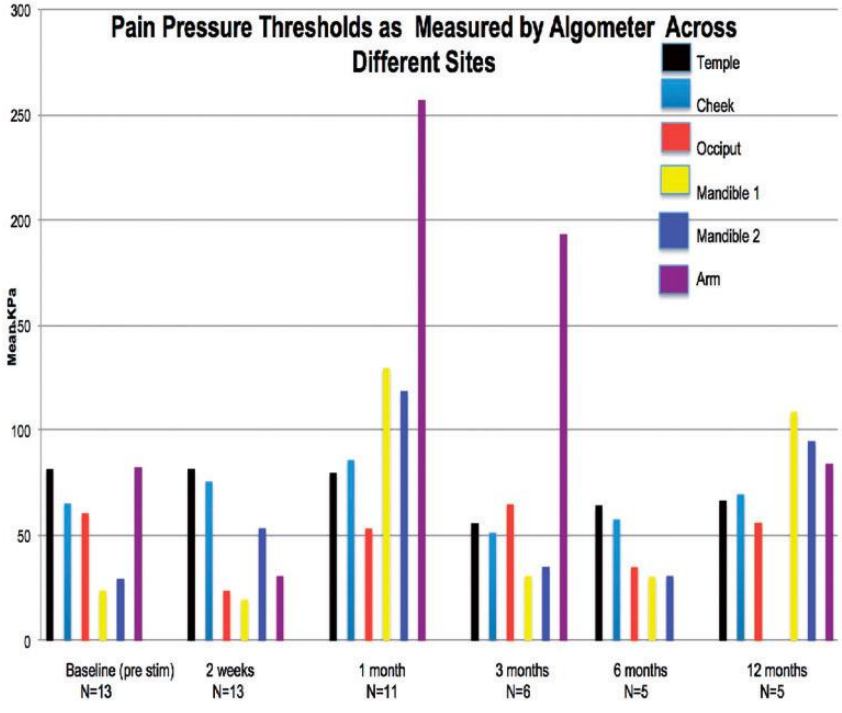
Methods: Following local regulatory approval, thirteen patients undergoing ONS dual Octrode 90 cm leads; rechargeable IPG (St Jude) at Barts Neuromodulation Unit, St Bartholomew's Hospital, London UK, were recruited to have Quantitative Sensory testing (QST) pre and post procedure 2 weeks, 1, 3, 6 and 12 months.

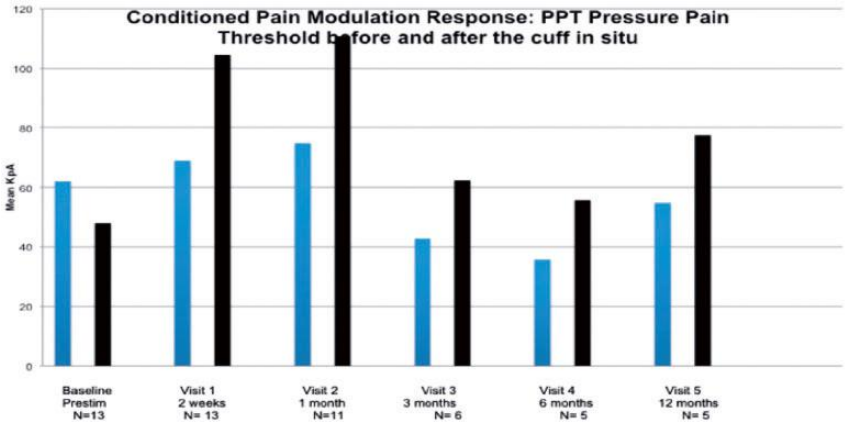
Results: Patients with intractable migraine demonstrated impaired CPM, (Pressure Pain Thresholds; PPTs 61.98 kPa vs 48.01kPA cuff inflated) prior to ONS; reverting to 'normal' CPM response within two weeks following ONS implant (68.9kPA vs 104.5kPA cuff inflated) continuing positively over the next 12 months. In contrast no statistical difference was observed in PPTs.

Conclusion: This is the first reported observation highlighting the effects on central sensitization following ONS. A consistent and sustained improvement in CPM was observed in contrast to PPT's where there was no difference. Normalisation of the CPM response following ONS indicates that the treatment may reduce central sensitization in migraine population without any change in the pressure pain thresholds peripherally.

Ref:1. Boyer N, Pain. 2014;155: 1196–205







PO475

Headache pathophysiology and imaging

Abnormal connectivity within executive resting-state network in migraine with aura

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Objective: we have previously demonstrated a disrupted fronto-parietal network connectivity in patients with migraine without aura. To evaluate the fronto-parietal network connectivity integrity in patients with migraine with aura, in the interictal period, in comparison to patients with migraine without aura and healthy controls.

Methods: using resting-state functional magnetic resonance imaging, we compared fronto-parietal network functional connectivity in 20 patients with migraine with aura versus 20 sex and age-matched patients with migraine without aura and 20 healthy controls, and assessed the correlation between fronto-parietal network functional connectivity and clinical features of patients with migraine. We used voxel-based morphometry and diffusion tensor imaging to investigate potential structural or microstructural changes.

Results: neuropsychological data revealed no significant executive dysfunction in patients with migraine. Resting-state functional magnetic resonance imaging showed that patients with migraine with aura, compared to healthy controls, had significant reduced fronto-parietal network functional connectivity which was independent of morphological differences and did not significantly correlate with clinical parameters. Conversely, there were no significant differences in the fronto-parietal network functional connectivity between patients with migraine with and without aura ($p < 0.05$, cluster-level corrected).

Conclusions: our data demonstrate a disrupted fronto-parietal network functional connectivity in patients with migraine with and without aura, in the interictal period. Although this functional phenomenon is present in the absence of clinically relevant executive deficits, it may reflect a vulnerability to executive high-demanding conditions of daily living activities in patients with migraine.

PO476

Headache pathophysiology and imaging

Molecular markers as predictors of efficacy of onabotulinumtoxin type a treatment in chronic migraine

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Background: The mechanisms associated to efficacy of onabotA in chronic migraine (CM) are unknown, and there are not predictor factors to response.

Aim: To study the efficacy of OnabotA in relation to molecular markers of inflammation (IL-6, TNF-alpha), endothelial dysfunction (PTX-3, ET-3), blood-brain barrier disruption (cFN), and trigeminovascular activation (CGRP, VIP) in patients with chronic migraine.

Method: We prospectively studied 50 patients with CM (44.3 ± 11.4 years; 98.0% women) (HIS 2013 criteria) treated with OnabotA (PREEMPT protocol). Patients were classified as moderate responders (improvement between 33–66% on the frequency of crisis or the reduction of headache intensity), excellent responders (improvement >66%) or non-responders (<33% or without improvement). Serum levels of IL-6, TNF-alpha, PTX-3, ET-3, cFN, CGRP and VIP were determined in blood samples obtained before OnabotA treatment.

Results: Non-responder CM patients were 15 (30%). By contrast, 28 patients (56%) were classified as moderate responders and the 14% (7 patients) were excellent responders. Excellent responders showed higher serum levels of PTX3 (1457.1 ± 460.1 vs. 1415.37 ± 476.8 vs. 720.3 ± 334.1 pg/mL; $p < 0.0001$); CGRP (180.4 ± 61.4 vs. 103.5 ± 82.7 vs. 58.2 ± 91.7 ng/mL; $p = 0.009$); cFn (19.3 ± 5.9 vs. 12.2 ± 5.1 vs. 14.3 ± 6.1 μg/mL; $p = 0.014$); and TNF-α (24.9 ± 44.6 vs. 7.6 ± 3.2 vs. 6.9 ± 2.4 pg/mL; $p = 0.039$) than moderate responders and non-responder CM patients, respectively. Likewise, moderate responders also showed higher serum levels of PTX3 (1415.37 ± 476.8 vs. 720.3 ± 334.1 pg/mL; $p < 0.0001$) than non-responder CM patients. No significant differences were found for the other biomarkers.

Conclusion: These results suggest that CGRP, cFn, TNF-α and especially PTX3 could be good predictors of onabotA response in CM patients.

PO477

Headache pathophysiology and imaging

The sound-induced flash illusions in menstrual migraine: a pilot study

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Background: The sound-induced flash illusions (SIFI) represent a valid tool to explore multimodal perception and are critically dependent on visual and acoustic cortical excitability [1]. In a previous study [2], we observed a significant reduction of illusions in migraine patients with respect to healthy controls, probably due to a condition of visual cortex hyperexcitability.

Objectives: Our aim is to evaluate SIFI perceptions in healthy women and patients with menstrual migraine and to describe the effects of cyclical change of steroid hormones and cortical responsiveness.

Methods: 19 women (11 affected with menstrual migraine, 8 healthy controls) were enrolled. Serum determination for sexual hormones (estradiol, progesterone) and a SIFI trial were performed in all participants in two different sessions on the 14th and 27th day of menstrual cycle.

Results: Healthy women show more illusions in the premenstrual (27th day) than in the luteal phase (14° day) ($p < .01$). Migraine patients don't show any difference during the two phases of menstrual cycle.

Conclusion: Results in healthy subjects are in line with hormonal effects on cortical excitability. During late follicular phase, the increase of estradiol could determine visual cortex hyperexcitability corresponding to a reduction of SIFI. Conversely, premenstrual fall of estradiol would account for restored illusions. Persistence of a reduced illusory susceptibility in both phases of menstrual cycle in migraine patients would underlie a reduced responsivity of visual cortex to hormonal fluctuation.

[1] Bolognini N, Rossetti A et al. Neuropsychologia. 2011;49231–7.

[2] Brighina F, Bolognini N, Cosentino G et al Neurology, in press.

PO478

Headache pathophysiology and imaging

Spreading depression at cellular resolution

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Cortical spreading depression (CSD) is still incompletely understood. We used *in vivo* two-photon microscopy, and whole cell, field potential and potassium recordings to study cellular events during CSD in mice.

At the cellular level, CSD was heterogeneous. The earliest detectable changes occurred ahead of the classical CSD wavefront: sub-threshold neuronal membrane

depolarizations up to tens of seconds before the larger depolarization of CSD, and calcium transients <1 second before arrival of the wavefront. With arrival of the wave, neurons underwent action potential firing on the way to complete depolarization. The duration of action potential trains corresponded closely to the rise time of extracellular glutamate, and was significantly faster than the rise time of extracellular potassium. The neuronal calcium transient lasted ~1 minute – similar to extracellular potassium. Transients varied between principal cells and interneurons, and also by distance to penetrating arterioles. Astrocytes underwent a brief (20–30 s) variable calcium transient whose duration was similar to that of glutamate elevation. Like astrocytes, arterioles had a variable response to CSD, but most underwent a biphasic constriction followed by dilation. The classic DC shift in local field potential lasted slightly longer than most cellular events. Surprisingly, the longest lasting event was membrane depolarization in individual neurons, which could last several minutes.

Our data provides a deeper understanding of CSD as a complex multicellular phenomenon that differentially and coordinately involves neurons, astrocytes and blood vessels. It also highlights the fundamental role of glutamate as well as potassium in the ignition and propagation of the phenomenon.

PO479

Headache pathophysiology and imaging

Different patterns of cortical excitability in medication overuse headache and chronic migraine: evidence by the sound-induced flash illusions

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Background: Responsiveness of visual cortex play a determining role in neural processes underlying multisensorial integration. The complexity of such an integration can be evaluated by sound-induced flash illusions (SIFI). As already shown by Bolognini et al. in healthy subjects, anodal transcranial direct current stimulation (tDCS) over occipital cortex reduces SIFI; according to our previous evidence, migraine patients are less prone to SIFI, especially during the attack.

Aim: On such a basis, we expected patients with chronic migraine(CM) to be less prone to SIFI as well as ictal episodic patients.

Methods: We recruited 65 patients (10 M, mean age ± SD 38.5 ± 11.8), including 54 patients with Medication Overuse Headache (30 patients with NSAIDS overusers, 24 triptan overusers) and 11 patients with CM. 64 patients with episodic migraine, 32 with- and 32 without-aura (42 F, mean age 32,3 ± 16), 20 healthy controls (13 F, mean age 38 ± 18) were enrolled. The experimental task consisted of reporting the number of flash seen on a black screen in isolation or in combination with beeps.

Results: All migraine groups showed significantly less SIFI than controls ($p < .01$); illusions were more reduced in chronic migraine than in episodic migraine and healthy controls, particularly in those overusing triptans ($p < .04$).

Conclusions: SIFI represent a valid tool to explore visual cortex excitability in episodic and chronic migraine. Chronic migraineurs show a reduction of SIFI like episodic patients during the ictal phase. Triptan overusers show less illusions due to an increase of excitability probably associated with a downregulation of 5HT1 receptors.

PO480

Headache pathophysiology and imaging

When the side matters: asymmetrical cortical hyperexcitability in cluster headache

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Background: Cluster headache (CH) is a severe primary headache disorder, whose pathophysiological processes remain largely unknown. Along with central disinhibition of the trigeminal nociceptive system and hypothalamic impairment, a cortical involvement has been supposed.

Aim: To evaluate cortical excitability in episodic CH patients by using different paradigms of transcranial magnetic stimulation (TMS).

Method: Twenty-five patients with episodic CH and thirteen healthy subjects underwent an experimental session where we evaluated, in both hemispheres, motor-cortical response to: 1) single-pulse TMS: i.e. motor threshold

(MT); input-output (IO) curves and cortical silent period (CSP) and 2) paired-pulse TMS: i.e. intracortical facilitation (ICF) and short intracortical inhibition (SICI). Thirteen patients were evaluated outside bout, while the remaining twelve patients were inside bout at the time of recording.

Results: We showed increased ICF values in the hemisphere ipsilateral to the side of pain in patients evaluated both outside and inside bout. Differently, IO curves showed increased slope in both hemispheres in patients examined outside bout, but only in the hemisphere contralateral to the affected side in those evaluated during bout.

Conclusion: Our results show a condition of increased cortical excitability in episodic CH both outside and inside bout. Interestingly, cortical excitability was greater in the hemisphere ipsilateral to the side of pain in patients outside bout, but decreased in patients inside bout possibly due to activation of compensatory inhibitory mechanisms of cortical excitability. Along with subcortical and peripheral mechanisms, changes in cortical excitability could also play an important role in the pathophysiology of CH.

PO481

Headache pathophysiology and imaging

Pain processing modulation in patients with migraine with and without ictal allodynia: a whole brain bold-fMRI study during trigeminal stimulation

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Objective: To investigate functional response of pain processing pathways constituting descending pain modulatory system and trigemino-thalamo-cortical nociceptive pathway related to trigeminal heat stimulation in patients with episodic migraine without aura experiencing allodynia during migraine attacks (MwoA + A).

Methods: Twenty patients with MwoA + A underwent whole-brain BOLD fMRI during trigeminal heat stimulation at three intensities. The functional response of neural pathways to this stimulation in patients with MwoA + A was compared with age- and sex-matched patients with episodic migraine without aura whitout ictal allodynia (MwoA-A) and healthy controls (HC). Secondary analyses explored associations between BOLD signal change and clinical features of migraine in patients.

Results: We observed a robust cortical pattern of BOLD signal change in response to trigeminal heat stimulation across all participants. Patients with MwoA + A showed a significantly increased activation in middle frontal gyrus (MFG) during moderate-noxious stimulations (51°C), in comparison with both patients with MwoA-A and HC. Furthermore, during high-noxious stimulation (53°C) a significantly decreased activation bilaterally in the secondary somatosensory cortex (SSC) has been observed in patients with MwoA-A compared to both patients with MwoA + A and HC. Here, a significant decreased activation has been shown in patients with MwoA + A compared to HC.

Conclusions: We provide novel evidence for cortical functional response to noxious trigeminal stimulation in patients with MwoA + A. These functional abnormalities in descending pain modulatory system and trigemino-thalamo-cortical nociceptive pathway may contribute to allodynia in patients with migraine, likely subtended by a failure in the analgesic compensatory reorganization.

PO482

Headache pathophysiology and imaging

Migraines and the concept of hidden depression (case report)

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Motivation of topic: Headaches, beyond the neurological component, which involves disturbances of cerebral microcirculation, may be regarded from the psychiatric point of view, particularly when the therapeutic arsenal of anti-inflammatory medication, painkillers and antimigraine is no longer given therapeutic results.

Objective: emphasizing a hidden depression of a 34 years old female patients, diagnosed with migraine crisis about ten years, whose evolution was significantly favorably influenced by dual type antidepressants.

Hypothesis: We assume that hidden depression symptoms are based on the patient's a family history, (for psychiatric disorder affective type), as well as important triggers thereof working life, related directly to personality structure, perfectionist, inclined to high goals and socially successful.

Methodology: cerebral CT, EEG (including during a headache episode), neurological exam, psychiatric interview, psychodynamic interview, neurological and psychiatric monitoring of daily evolution under treatment, map of life, psychological tests.

Results: Neurological, diagnosis is headache seizures. Psychiatrically, we can discuss about two concepts: hidden depression and Algic disorder. Psychodynamic, patient functioning is marked by repression and discharge mechanisms. Therapeutically, emphasize sensitivity (negatively) to SSRI's (by emphasizing headache), neutrality versus tricyclic antidepressants amitriptyline and type net favorable response, with quick time action (about a week) Venalfaxină.

Conclusions: The concept of hidden depression is one of the certainty dates, being partly identified DSM IV TR diagnosis Algic Disorder and partially explaining headache episodes, of the present patient. Rapid response to dual antidepressant, and maintenance of the well being, absence of marked intensity seizures, support the efficacy of combination therapy (analgesic, anti-inflammatory and antidepressant).

PO483

Headache pathophysiology and imaging

Central nociceptive impairment data in chronic migraine and chronic orofacial pain

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Objective: Previous studies have suggested the presence of central nociceptive impairment in chronic migraine(CM) and chronic orofacial pain(COP) attributed to temporomandibular disorders(TMD), but available results are conflicting. Additionaly, chronic pain comorbidity, such as anxiety or depression are known to affect pain sensitivity. Our aime was to investigate central sensitization, disability and psychiatric comorbidity in patients with CM and COP attributed to TMD compared to healthy subjects

Methods: Cross-sectional observational study with 33 subjects suffering from CM, 23 heterogeneous COP and 26 matched healthy controls. Bilateral multi-segmental pressure pain thresholds (PPTs), temporal summation of pain (TSP), and information about duration-of-pain history, Neck Disability Index (NDI), Craniofacial Pain Disability Inventory (CF-PDI), Beck Depression Inventory (BDI) and State Trait Anxiety Inventory (STAI) scores were analyzed.

Results: 82 participants (79 women), mean age, 47.2 years (21–70). On average, there were significant differences in PPTs (all sites: $P < .001$), TSP (all sites: $P < .009$), NDI($P < .001$), CF-PDI($P < .001$) and BDI score ($P < .02$) in patients with CM and COP as compared to healthy controls. Nevertheless, there were no significant differences in the magnitude of PPT decreases, as well as in TSP and BDI between both groups ($P > .05$). PPT levels over distant pain-free areas were positively correlated to PPTs over trigemino-cervical areas ($P < .01$). Additionally, positive correlation between duration-of-pain history and TSP was found ($P < .05$).

Conclusions: The results revealed bilateral widespread pressure pain hypersensitivity in patients with CM and COP attributed to TMD. These findings support the view that central sensitization mechanisms are involved in both conditions.

PO484

Headache pathophysiology and imaging

Neurovascular contact in trigeminal neuralgia. A comparison between 3T and 1.5T MR imaging

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Background: Trigeminal neuralgia is frequently associated with neurovascular contact (NVC). MR imaging is widely used for assessment of NVC. The sensitivity of 3 T scanners appears to be higher than 1.5 T for the diagnosis of NVC.

Aim: To compare the diagnostic accuracy of high-resolution 3D-CISS MRI at 3 T compared with 1.5 T for assessment of NVC.

Methods: Retrospective review of 87 patients with the diagnosis of trigeminal neuralgia from June-2012 to January-2015. 22 patients were excluded because in 18 of them MRI was performed in another hospital and 4 patients were not scanned.

65 patients had undergone a brain MRI, 13 without CISS sequences and 52 with CISS sequences, acquired on a 1,5 T (75%) and 3 T (25%) MRI.

Results: A total of 65 patients were included, with a mean age of 58.32 years (55.82–60.82). 46 were female (70.76%).

In none of the 13 patients without 3D-CISS sequence was observed a neurovascular contact.

Of the 52 patients, 40 (76,92%) had neurovascular contact; 13 patients had 3 T-MRI (with 3D-CISS) and 10 (76,92%) had neurovascular contact; 39 had 1,5-T MRI (with CISS) and 30 (76,92%) had neurovascular contact associated with the neuralgia.

Conclusions: Neurovascular contact is commonly associated with trigeminal neuralgia.

Our finding suggest that NVC was correctly identified in 3D-CISS sequence using 3T and 1.5 T. we did not find any difference between 3 T and 1.5 T MRI.

PO485

Headache pathophysiology and imaging

Brain arterio-venous malformations (BAVM) with dural arterial supply: effect of dural supply obliteration on headaches

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Background: Brain arterio-venous malformations (BAVM) with pure dural or mixed parenchymal and dural arterial supply present frequently with headaches. The mechanisms that lead to these headache are still poorly understood. Headaches seem to disappear after complete or partial obliteration of dural arterial supply only.

Aim: To systematically analyze the effect of endovascular obliteration of the dural arterial supply on headaches in a consecutive series of BAVMs with both, parenchymal and dural arterial supply presenting with headaches. Mechanisms of pain and relief of headaches by occlusion of the dural supply are to be discussed and my help to explain headache pathophysiology.

Materials and methods: In a consecutive series of 5 patients with BAVM presenting with headaches, patients exhibiting parenchymal and dural arterial supplies were analyzed before and after endovascular treatment of the dural component only.

Results: In all cases, a partial or complete arterial obliteration resulted in a significant improvement or complete persistent relief of their headache symptoms and could be performed without significant complication.

Conclusion: In BAVM patients presenting with headaches and exhibiting a mixed dural and parenchymal arterial supply, the endovascular obliteration of the dural supply was performed at low procedural risk, little impact on BAVM hemorrhagic risk evolution and good symptom relief. A targeted, partial endovascular treatment in such BAVM may be considered as symptomatic treatment.

PO486

Headache pathophysiology and imaging

Intensity-dependence of cortical auditory evoked potentials: correlation with female sex hormones

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Background: Intensity-dependence of cortical auditory evoked potentials (IDAP) is on average increased in migraineurs between attacks. IDAP is thought to be inversely related to serotonin (5-HT) transmission, but it is not known if this is influenced by the menstrual cycle and sex hormones.

Aim: To analyze the correlation between IDAP, the menstrual cycle, and blood levels of estradiol (E2) and progesterone (P4) in female migraineurs.

Methods: Auditory Evoked Potentials were obtained at four different stimulation intensities in 20 patients suffering from migraine without aura (MO) both during menses and at mid-cycle. For each intensity 120 trials were averaged off-line. IDAP was expressed by the amplitude/stimulus intensity function (ASF slope) for global and block averages and correlated with plasma E2 and P4 levels.

Results: There was no significant difference in IDAP slopes between mid-cycle and menstrual recordings in migrainous women. Moreover the IDAP slope values at both time periods were significantly correlated ($R = 0.803310$; $p = 0.000020$). Nor significant correlation was found between IDAP slopes and E2 or P4 plasma levels.

Conclusion: IDAP slope seems not to be influenced by the menstrual cycle. It is not correlated with plasma levels of female sex hormones. The hormonal cycle is thus not a confounding factor when IDAP is used for diagnostic purposes.

PO487

Headache pathophysiology and imaging

Sleep disturbances in headache patients

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Objectives: Evaluation of clinical features of headache during sleep-wake cycles in patients with cluster headache (CH) and migraine and improvement of medical care for headache patients with sleep disorders.

Rationale: CH and migraine-related pain depends on patient's baseline condition during the sleep-wake cycle. CH and migraine significantly impair patient's physical performance and cause a considerable financial damage.

Materials and Methods: 38 patients (20 CH and 18 migraine patients) and 22 healthy reference subjects were examined using clinical, psychological, neurophysiologic methods, and questionnaires.

Results: CH patients presented severe disorders of sleep architecture with absence of REM sleep before and after the pain attack and shift of the delta sleep stage with its prolongation in the morning after attacks. During the remission their sleep architecture was almost normal. In migraine, the following sleep disorders were found during the pain attack and in remission: absence of REM before and after pain episode; absence of the delta sleep stage; difficulty falling asleep; increased nocturnal wakefulness; frequent movements in sleep, and prevalence of superficial sleep. The time of the episode onset significantly affects the severity of pain attacks: CH and migraine episodes are more severe during sleep than during wakefulness.

Conclusion: The study demonstrated relations between HA and sleep disorders in migraine and CH patients. Regional centers should be established to study sleep disorders and their effect on HA and to improve the quality of medical care. A complex approach to management of sleep disorders should be applied there with involvement of a multidisciplinary team.

PO488

Headache pathophysiology and imaging

Mitochondrial dysfunction in the development of trigeminal sensitivity in a rat model of chronic migraine and the spontaneous trigeminal allodynia rat model

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Background: Impairment of mitochondrial function has been observed in migraine patients and a rat model of chronic migraine.

Aim: To further characterize mitochondrial dysfunction in a rat model of chronic migraine and the Spontaneous Trigeminal Allodynia rat model.

Methods: Trigeminal sensitivity was determined with von Frey monofilaments. qPCR gene-chip recorded mRNA changes. Mitochondrial respiration was measured in the trigeminal nucleus caudalis (TNC) brain sections using the Seahorse XF analyzer. Glutamate was measured in the TNC using *in vivo* microdialysis following treatment with GTN and perfusion of rotenone, an electron transport chain (ETC) complex I inhibitor.

Results: CoQ10 prevented sensitization. Acetate increased sensitization in both rat models. Significant modulation of mitochondrial related genes was seen. Spare respiratory capacity was decreased in both rat models. Sensitized rats did not utilize acetate as efficiently as naive rats, whereas succinate was used similarly. In the presence of rotenone, glutamate levels in the TNC of naive rats increased to levels seen in sensitized rats following GTN.

Conclusions: Genetic analysis suggests changes in mitochondrial function in the TNC of sensitized rats. Acetate increased periorbital sensitivity while supplementing mitochondrial function with CoQ10 prevented sensitivity. A decreased spare respiratory capacity was seen in both animal models. Differential utilization of acetate and succinate suggest malfunction of complex I of the ETC. Rotenone increased glutamate levels to that seen in sensitized rats following GTN. These data indicate that decreased mitochondrial function within the TNC contributes to the development of chronic trigeminal pain, likely via increased extracellular glutamate.

PO489

Headache pathophysiology and imaging

Prevalence of right to left shunt (RtLS) in women with migraine is not related with frequency of attacks

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Background: Prevalence of RtLS is estimated as 25% of the general population. In previous studies, this prevalence has been found to be increased in migraine with aura and in chronic migraine.

Aim: To study the prevalence and pathophysiology of RtLS in a series of women with episodic (EM) and chronic migraine (CM).

Methods: This series includes 127 women (age 44 years, range 16–68) meeting diagnostic criteria for CM and 54 women (age 39 years, range 16–66) for EM. We carried out a transcranial doppler study (AplioXG, model SSA-790 A, Toshiba) following the CODICIA study protocol.

Results: In CM, 68 patients (53%) showed some degree of RtLS whereas in EM 29 patients (54%) had RtLS. In CM the prevalence of RtLS was 59% in patients with aura and 48% in patients without. In EM the prevalence of RtLS was 54% in patients with aura and 52% in patients without. In CM, RtLS was permanent in 24% and massive in 20% of the patients. In EM, RtLS was permanent in 35% and massive in 37% of the patients.

Conclusion: In our series the prevalence of RtLS is higher than the expected for the general population both in EM and CM. We did not find differences in the prevalence, degree or appearance at rest or after Valsalva of RtLS in relation with frequency of attacks (EM versus CM) or aura status.

PO490

Headache pathophysiology and imaging

Influence of migraine frequency in subclinical brain lesions

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Background: The prevalence of posterior circulation infarcts and white matter hyperintensities is increased in migraine patients. The frequency of migraine attacks may increase the risk of subclinical brain lesions.

Aim: To determine whether subclinical brain lesions are more frequent in chronic migraine (CM) than in episodic migraine (EM) patients.

Methods: We performed a retrospective review of all patients with CM and EM attended between September 2013 and September 2014 with ages between 18 to 67 years. We selected those patients in which brain MRI was performed. MRIs were acquired on a 1,5 T (3–5 mm slices) and 3 T unit (3 mm slices). Brain images were analyzed by neuroradiologists.

Results: Two hundred and forty three patients were included, 129 with CM and 114 with EM. In CM patients only 0,78% had posterior circulation infarcts and 17,72% had hemispheric white matter hyperintensities. Among the patients with EM 2,73% had posterior circulation infarcts and 28,77% had hemispheric white matter hyperintensities.

Conclusion: We found posterior that posterior circulation infarcts and white matter hiperintensities are less frequent in CM than in EM. Our results suggests that migraine attack frequency does not increase the risk of subclinical brain lesions.

PO491

Headache pathophysiology and imaging

The prevalence of right to left shunt (RtLS) is not related with white matter hyperintensities in chronic migraine (CM)

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Background: Patients with migraine have been reported to be at increased risk of white matter lesions (WMLs). This risk was higher in patients with aura and with higher frequency to attacks.

Aim: To determine wether in CM patients the presence of RtLS is related with an increased risk of WMLs on MRI.

Methods: This series includes 88 women (age 43 years, range 16–68) meeting diagnostic criteria for CM. We carried out a transcranial doppler study (AplioXG, model SSA-790 A, Toshiba) following the CODICIA study protocol. Brain MRIs were acquired on a 1,5 T unit Signa LX 9.1 (General Electrics Systems, USA). Protocol includes whole brain weighted images in saggital T1 (5 mm slides), axial FLAIR T2 (3 mm) and combined proton density and T2 fast spin echo (3 mm).

Results: 46 out of 88 patients had some degree of RtLS. The prevalence of WMLs in patients with RtLS was 65% (30 out of 46), whereas in patients without RtLS it was 59,5% (25 out of 42). In patients with RtLS and aura the prevalence of WMLs was 76% and in patients with RtLS without aura the prevalence was 52,3%.

Conclusion: In our series of CM patients there were not differences in the prevalence of WMLs according to RtLS status. However, in patients with CM and aura, RtLS was related with a higher frequency of WMLs.

PO492

Headache pathophysiology and imaging

Insulin-induced hypoglycemia modulates trigeminovascular nociceptive transmission: implications for insulin-resistance and obesity in migraineurs

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Background: A clinical association between migraine and altered glucose metabolism has been hypothesized. Insulin-resistance is correlated positively with CGRP levels and contributes to the pathogenesis of obesity. Furthermore, obesity is associated with increased frequency and intensity of migraine. Orexins are known to be involved in both obesity and migraine pathophysiology and insulin-induced

hypoglycemia increases prepro-orexin mRNA hypothalamic expression.

Aim: To determine the effect of insulin-induced hypoglycemia on dural-evoked nociceptive trigeminovascular activation.

Methods: Sprague-Dawley rats were anesthetized, the parietal bone overlying the middle meningeal artery was removed for electrical stimulation of the dura mater. Electrophysiological recordings were made from trigeminocervical complex (TCC) neurons. Rats received human insulin (10 U/kg, i.v.) or sterile water as control. Glycemic levels were monitored throughout the experiment. Studies approved by IACUC and followed NIH guidelines.

Results: Administration of human insulin significantly reduced nociceptive dural-evoked Aδ-fiber neuronal firing in TCC ($F_{8,80} = 6.6$, $p = 0.000$), reaching a maximum inhibition of 17% at 25 minutes. Although insulin produced modest reductions in spontaneous background activity, these effects did not reach statistical significance. Blood glucose levels significantly reduced after insulin administration, comparing to pre-injection levels ($F_{7,56} = 23$, $p = 0.000$).

Conclusion: These data demonstrate that a 'fast and long action'' insulin significantly inhibits dural-evoked nociceptive neuronal firing in the TCC, an effect preceded by hypoglycemia. Increases in circulating insulin levels most likely activate hypothalamic nuclei involved in descending modulation of trigeminovascular firing, and may explain some part of the effects which may be the basis of this response.

PO493

Genetics and biomarkers of headache disorders

Involvement of THR698THR (nt2369) polymorphism on CACNA1A gene in common type of migraine in iranian patients

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Background: Migraine is a prevalentneurological disturbance with the incidence of 16% of general population. Familiar hemiplegic migraine (FHM) is one of the most powerful congenital migrainesorts of headache which is a rare autosomal dominantly inherited subtype ofmigraine with aura that many studies revealed association this kind of migrainewith mutations in the *CACNA1A* gene in different ethnic groups.

Aim: The aim of this study was tosurveyed leukocyte genomic DNA mutation of *CACNA1A* in Iranian migraine-patients with and without aura who have family history of migraine.

Material and method: Weincluded 74 common migraine patients consequently. Headache severity wasevaluated according to Headache Impact Test (HIT6) questionnaire and quality oflife of patients was investigated according to MSQ (Migraine-Specific Quality of Life Questionnaire v2.1) questionnaire. Thirty patients with positive familyhistory of migraine were selected and sequencing analysis after DNA extraction was performed

Result: Directsequencing revealed a known SNP G to A transition in the exon 16 (nt2369, G ?A) in 9 patients. There was no significantly correlation between polymorphismand type of migraine, severity, frequency, duration and quality of life infamily positive migraine. Evaluated migraine severity by HIT6 questioner couldn'tact as a risk factor for this polymorphism (OR: 0.93, CI%95 0.82–1.06 $P = 0.3$).

Conclusion: *CACNA1A*is most likelynot a major susceptibility gene for common migraine in Iranian maigrainous. It's essential to study more on larger series and covering all 47 exons of the *CACNA1A*gene to confirm this hypothesis.

PO494

Genetics and biomarkers of headache disorders

Assessment of serum level of vitamin d and resistin in patients with migraine

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Background: Migraine is a disorder, characterized by recurrent episodes of headache and associated symptoms. The interrelationship between migraine and vitam1in D deficiency has not been fully explored in the literature. resistin, an adipocytokine in humans, is synthesized predominantly by mononuclear cells. There is evidence demonstrating an association between migraine and processes associated with inflammation and immunity.

Aim: Determining serum level of vitamin D and resistin in patients With Migraine Attending to Hospital of Tehran comparing to healthy people in 2013.

Methods: In this case-control study 35 people with migraine attending to Clinic of Neurology and 35 healthy control in Fasting Condition were examined and Serum level of 25(OH) Vitamin D and resistin was measured in them with Eliza Assay.

Results: The mean level of serum 25(OH) vitamin D in patients was 31.60 ng/ml and was 33.29 ng/ml in healthy people ($p > 0.05$). The mean level of resistin in patients and controls was 16.26 ng/ml and 20.55 ng/ml ($p = 0.003$).

Conclusions: we found no significant differences between patients with migraine and healthy subjects with respect to serum level of vitamin D, nevertheless, our findings suggest the clinical relevance of vitamin D in context of severity of migraine. Notably, the current study presented novel data of decreased level of resistin as a putative biomarker in migraine patients.

Keywords: Migraine, Vitamin D, Resistin.

PO495

Genetics and biomarkers of headache disorders

Prevalence of genetic polymorphism rs11568817 in the promoter region of the gene 5-HTR1B in migraine patients compared with controls

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Background: Migraine is a common hereditary chronic neurovascular disorder, with a prevalence of about ten to fifteen percent of the adult population. Recently several evidences proved relation between genetic factors and migraine. One of the important genes involved in the pathogenesis of migraine is 5-HTR gene. The protein produced from this gene is a clinically important because it plays an important role in the occurrence and treatment of migraine.

Aim: This study was aimed to evaluate the prevalence of the rs11568817 polymorphism in the gene promoter region of the gene 5-HT1B in patients with migraine versus to the control group.

Method: 102 newly diagnosed migraine patients and 151 controls, matched for age, sex and socioeconomic status were enrolled in the study. Peripheral blood sample was used for DNA extraction. Genetic polymorphism rs11568817 in the promoter region of the gene 5-HTR1B were analyzed by using a HRM-PCR technique.

Result: Genotypes Frequency in both cases and controls were in accord with Hardy–Weinberg equilibrium. The alleles frequency of rs11568817 gene are significantly different between migraine patients and control subjects. (OR = 1.74, 95% CI: 1.038–2.941, P = 0.036)

Conclusion: This study showed that genetic polymorphism rs11568817 in the gene 5-HTR1B plays in susceptibility to migraine. This was the first study to assess the frequency of this polymorphism in migraine patients. More studies with larger sample size are needed to further establish the role of 5-HTR gene in patients with migraine.

PO497

Genetics and biomarkers of headache disorders

Lack of dementia in severe migraine sufferers.: is there a possible explanation?

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Introduction and Aim: In 2006 we presented preliminary data concerning a population of over 2000 migraine (M) suffers and a similar matched control group. Subjects were observed by using MRI when 55 years old till to their death. M sufferers differ from primary pain exempt subjects since they were nearly (2% maximum peak) exempt from dementia at any age. Aim: to understand the possible determinants of such a result by analysing variables which includes also changes in nitric oxide (NO), Substance P (SP) and Calcitonin- gene-related peptide (CGRP) we first show to increase during headache attacks

Methods and Results: The observation was carried out on 2538 M sufferers and 2489 subjects personally and familiarly exempts from any primary pain and on 20 M suffers 30 years old. Demographic, social/cultural and psychometric variables were non significant (MANOVA). NO level decreased with age, nevertheless, during attacks plasma peak values of the gaseous messenger remained high ($p > 0.0001$ versus baseline). Similarly enhanced serum, saliva SP-LI and CGRP-LI (both $p > 0.0001$ versus baseline, NS versus 30 years old sufferers)

Conclusion: NO is thought to play a role in multiple forms of use-dependent synaptic plasticity, SP-LI is known to be severely lowered in five of eight brain regions of subjects suffering from Alzheimer disease/senile

dementia, CGRP-LI is known to be lower in dementia. The observed M attack-induced increase of tachykinins and messengers seemingly maintain brain at a good functional level. If so, problems may be related over-use of to drugs likely erasing M sufferers neuronal auto-defence system.

PO498

Genetics and biomarkers of headache disorders

Association of genetic factors influencing serum metabolites with genetic risk for migraine

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As part of an ENGAGE (European Network for Genetic and Genomic Epidemiology) flagship project, we have performed a large genome-wide association (GWA) study in 7478 individuals of European descent for 129 serum metabolites (measured via mass spectrometry on a quantitative metabolomics platform at Biocrates Life Sciences AG).

To identify new and potentially relevant biological processes and pathways involved with migraine aetiology, we tested for association between genetic factors influencing these serum metabolites and genetic risk for migraine (Suhre et al. 2011).

We first applied the new SECA approach (Nyholt 2014) to assess whether genetic risk factors influencing serum metabolites are correlated with the genetic risk for migraine identified in the recent International Headache Genetics Consortium (IHGC) GWA meta-analysis of 23285 migraine cases and 95425 controls (Anttila et al. 2013). We next tested whether the metabolite associations differ between migraine with aura (MA) and migraine without aura (MO), and between females and males. Genetic risk factors influencing serum metabolites found to be associated with genetic risk for migraine were further investigated in a subset of individuals with serum metabolite measures for whom migraine status is available.

Our results implicate new biological processes and pathways involved with migraine aetiology.

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PO499

Genetics and biomarkers of headache disorders

The association of vitamin d receptor single nucleotide polymorphism in children and adolescents with migraine and tension type headaches

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Objectives: Vitamin D acts on human body through vitamin D receptor (VDR). FokI single nucleotide polymorphism (SNP) seems to have the greatest influence on VDR function. In other studies FokI SNP was associated with the influence on calcium homeostasis and vitamin D absorption. It also has impact, as one of the factors, on bone mass density and osteoporosis formation. Up to date no studies were done on Polish population with headaches.

Materials and Methods: In a group of 45 patients, 18 with migraine and 27 with tension type headaches, three VDR polymorphisms were evaluated– FokI (rs2228570), BsmI (rs1544410) and TaqI (rs731236) using Taq-man method. The results were compared to the data obtained from healthy Polish population and migraine population from other countries.

Results: In the migraine group we found 6 CC FokI patients, 6 TC patients and 6 TT patients (wild-type). In the tension type headache group 7 patients were CC FokI type, 12 – TC and 5 – TT. Concerning TaqI polymorphism CT type was the most common (48% of patients). In the studied group GA type of BsmI was the most common and associated with CT TaqI type.

Conclusions: In Polish healthy population FokI TC type dominates in 53%, the rate is similar in tension type group, yet differs in migraine group. The study is ongoing and more patients are being recruited. Although a recent review shown no correlation of vitamin D deficiency with headaches there are only a few studies on the topic and it requires further investigation.

PO500

Genetics and biomarkers of headache disorders

Migraine and oxidative balance evaluation with d-ROMS and BAP test

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Background: An impairment of mitochondrial oxidative metabolism might play a role in the pathophysiology of the migraine. However, data are in part controversial and the possible underlying mechanism remain elusive to date and the data regarding the interictal state in migraineurs is limited.

Aim: To evaluate the oxidative balance in a sample of patients with migraine by means of routine specific serum tests, such as d-ROMs test and BAP test.

Methods: 150 outpatients, (92 F/58 M) mean age 35.8 years(SD 12.8), range 18–64 years, suffering from migraine without aura (ICDH-II 2004 criteria) were enrolled. The mean duration of disease was 1.9(SD 0.7) years. Serum total oxidant capacity was determined by performing the d-ROMs test, which chemical principle is based on the ability of a biological sample to oxidize N,N-diethylpara-phenylenediamine (normal range 250–300CARR-U, where 1 CARR-U is equivalent to 0.8 mg/L H_2O_2), while serum total antioxidant capacity was assessed by means of BAP test, which measures the ability of a serum sample to reduce iron from the ferric to the ferrous ionic form (optimal value $>$ 2200 micromol/L reduced iron).

Results: Mean values of d-ROMs tests were 392.4 CARR-U(SD 128.6) while mean values of BAP test were 1764.6micromol/L reduced iron(SD 526.6).

Conclusion: According to herein reported data, enrolled patients were found to be in a classical condition of oxidative stress. Although preliminary our study showed that migraine without aura is associated to oxidative stress and suggest that oxidative stress may represent a key event in the pathophysiology of migraine and a suitable therapeutic target.

PO501

Genetics and biomarkers of headache disorders

Migraine biomarkers in cerebrospinal fluid and blood: a systematic review and meta-analysis

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Background: Identifying biochemical biomarkers for migraine may help to unravel its pathophysiology. Especially biochemical changes in the cerebrospinal fluid (CSF) may reflect biochemical changes in the brain.

Aim: To identify compounds with altered concentrations in CSF and blood from migraine patients.

Method: Systematic review and meta-analysis. Studies measuring biochemical compounds in CSF from chronic and/or episodic migraineurs and non-headache controls were retrieved by searches in PubMed, EMBASE and Web of Science (August 16, 2014). Subsequent searches retrieved studies with blood measurements of selected CSF biomarkers. Two investigators independently assessed eligibility criteria. If there were three or more studies for one compound, results were pooled in meta-analysis with standardized mean differences (SMD and 95% C.I.) as effect measures.

Results: Sixty-two unique compounds were identified in 40 CSF studies. Most important and consistent results for CSF were increased concentrations of glutamate (5 studies, SMD: 2.22 [1.30, 3.13]), calcitonin-gene related peptide (CGRP) (3 studies, SMD: 3.80 [3.19, 4.41]) and nerve growth factor (NGF) (3 studies, SMD: 6.47 [5.55, 7.39]) in chronic migraine patients and decreased concentrations of β-endorphin (β-EP) in both chronic (4 studies, SMD: −1.37 [−1.80, −0.94]) and interictal episodic migraine patients (3 studies, SMD: −1.12 [−1.65, −0.58]). Blood concentrations were increased for glutamate (interictal) and CGRP (chronic, interictal and ictal) and decreased for β-EP (chronic, interictal and ictal).

Conclusion: Concentrations of glutamate, β-EP, CGRP and NGF are altered in CSF and, except for NGF, blood from migraine patients. Future research should focus on

the pathophysiological role of these compounds in migraine.

PO502

Genetics and biomarkers of headache disorders

Genetic screening and characterization of hyporcretin receptor 2 in cluster headache in Sweden

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Background: The pathophysiology of cluster headache is largely unknown and a causative role has been suggested for a genetic variation (G1246A) in Hypocretin receptor 2 gene (HCRTR2) in familial and sporadic forms. HCRTR2 is located on chromosome 6p12.1 and encodes a G-protein coupled receptor which is expressed exclusively in the brain.

Aim: We will screen G1246A in a Swedish case-control material and test for possible association with disease. We also aim at evaluating the possible effects of G1246A on the HCRTR2 mRNA structure and characterize HCRTR2 mRNA expression in rodent tissue.

Method: We screened cluster headache patients and healthy controls for G1246A using quantitative PCR. The possible effects of G1246A on HCRTR2 mRNA structure was evaluated using the software mfold. We have designed and tested HCRTR2 probes using in situ hybridization on rodent brain tissue.

Results: Preliminary genetic analysis showed no significant changes in allele frequency. However mRNA analysis shows 0.5–4.5% difference concerning secondary structure and energy for mRNA folding between sequences with the two different G1246A alleles. In situ data show HCRTR2 mRNA expression in hippocampus CA3, cingulate cortex and cortex layers.

Conclusion: We observed a difference concerning secondary structure and energy for mRNA folding energy between the G1246A wild-type and mutated sequence. These results suggest a possible effect on HCRTR2 gene function. We observed HCRTR2 mRNA expression in hippocampus, cingulate cortex and cortex layers in rodent brain tissue. A larger material needs to be screened before drawing conclusions on HCRTR2 involvement in cluster headache in Sweden.

PO503

Genetics and biomarkers of headache disorders

Sporadic hemiplegic migraine and cerebral oedema after minor head trauma: a unique CACNA1A gene mutation

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Background: Familial hemiplegic migraine (FHM) has been associated with mutations in CACANA1 gene coding for a calcium-channel subunit. Sporadic hemiplegic migraines (SHM) are only rarely reported to have mutations in this FHM gene.

Aim: To describe a unique *CACNA1A* gene mutation found in a patient presenting with a history of SHM and cerebral oedema after minor head injury.

Methods: Case report

Results: A 37 year old man with global developmental delay and a history of cerebellar ataxia was referred to our headache clinic with a history of "complicated headache attacks". Pregnancy was uneventful but by 6–12 months he was "floppy" and slow to meet developmental milestones. At 3 years, he was admitted to hospital in a coma following being hit on head with a toy car and diagnosed with cerebral oedema. He had multiple admissions with similar clinical events in early life with no cause was found. At 7 years he began to suffer from events consistent with hemiplegic migraine associated with hemiparesis and disturbances in his vision and speech but no loss of consciousness. Attacks would last days to weeks. Minor head injuries were a consistent trigger for these attacks. There was no family history of migraine with aura. Examination was consistent with a cerebellar syndrome. Brain imaging revealed cerebellar atrophy. Sequence analysis of *CACANA1A* identified an error in exon 25 (c.4055G > A) leading to the mutation p. Arg1352Gln. This mutation was absent in his parents.

Conclusion: A novel *CACNA1A* mutation is described in SHM induced by minor head trauma.

PO504

Genetics and biomarkers of headache disorders

Transcriptional activation of non-LTR retrotransposons specific transcripts in rats

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Objectives: Basic objectives were to analyze the transcriptional regulation of L1Rn elements in response to stresses.

Methods: Real time PCR analysis using RNA isolated from various brain regions and various tissues from old and young wistar rats was carried out to determine the change in L1 transcripts.

Results: There was no significant change in the expression of L1Rn in various brain regions of 2 month old and 18 month old rats except cerebral cortex.

The heavy metals nickel, cadmium, lead, mercury and aluminum upregulates the expression of L1 in tissue specific and age dependent manner.

Conclusions: The results of this investigation conclusively prove that LINE1 retroelements are transcriptionally activated in response to stress.

PO505

Genetics and biomarkers of headache disorders

Association of RAMP1 rs7590387 with transformation of episodic migraine into medication overuse headache

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The calcitonin gene-related peptide (CGRP) has a central role in the pathogenesis of migraine, however the possible contribution of polymorphisms in CGRP-related genes as pharmacogenetic determinants or as risk factors for chronification of episodic migraine has been poorly investigated. We herein investigated the role of polymorphic variants in CGRP-related genes looking at the association of rs3781719 in the calcitonin gene-related polypeptide-alpha (CALCA) gene and of rs548294 and rs2195450 at the receptor activity modifying 1 (RAMP1) locus with triptan response in patients with migraine without aura (MwoA). In addition, we evaluated the role of these polymorphisms as risk factors for transformation of episodic migraine into medication overuse headache (MOH). Genotyping was conducted retrospectively by Real-time PCR allelic discrimination assay in 219 patients with MwoA and 130 with MOH in whom migraine was the primary headache type. Gene variants association was evaluated by logistic regression analysis adjusted for clinical confounding factors, and the threshold of statistical significance for multiple testing was set at $P < 0.016$. No evidence of association was found between the three polymorphisms analysed and triptan response in MwoA patients. Conversely, carriers of RAMP1 rs7590387GG were found at lower risk of episodic migraine transformation into MOH (vs C allele carriers, OR: 0.27, 95%CI: 0.13–0.57, $P = 0.0002$). While our results exclude a clinically relevant impact of the SNPs investigated on headache response to triptans, our findings support a role of RAMP1 rs7590387 as susceptibility risk factor for transformation of episodic migraine into MOH.

PO506

Genetics and biomarkers of headache disorders

Genetic polymorphisms of the interleikin-6 receptor -183G/A in the patients with chronic headache

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Background: There are some hypotheses that an immunologicdysfunction has been involved in migraine pathogenesis. Interleikin-6 (IL-6) is a major inducer of the acute phase reaction in response to inflammation or tissue injury. The-183 G/A region is the binding site to NF-1 which is one of the transcription factor for IL-6 receptor (IL-6 R) and the polymorphism strongly influences the soluble IL-6 R level.

Aim: The aim of this study was to investigate the IL-6 R gene polymorphism in chronic headache. We analyzed polymorphisms of -183 G/A(rs4845617) in the promoter region.

Methods: Genotyping forIL-6 R -158 A/C polymorphism was performed in 65 patients with migraine with aura(MA; 44 females, average age: 32.6 years), 138 patients with

migraine without aura(MO; 111 females, average age: 36.8 years) and 77 patients with tension typeheadache (TH; 59 females, average age: 49.8 years) on leukocyte genomic DNA samples by PCR-RFLP) analysis. One hundred eighty three normal healthy volunteers composed the control group (CTL; 128 females, average age 58.1 years). The differences in the frequency of IL-6R alleles and genotypes between groups were evaluated by the gene-counting method and comparison of groups by thechi-square test. The level ofsignificance was set at p

Results: Thedistribution of IL-6 R genotype in patients and CTL did not deviate significantlyfrom the Hardy-Weinberg equibrium. The -158A-allelicfrequency of MO patients was significantly higher than that of CTL.

Conclusions: Ourresults indicate that IL-6 R -158 A/C polymorphism is a genetic risk factor forpatients with MO.

PO507

Genetics and biomarkers of headache disorders

Trigeminovascular dural vasodilation is affected in familial hemiplegic migraine type 1 knockin mice

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Background: Neuronal hyperexcitability has been shown in transgenic knockin mice carrying the familial hemiplegic migraine type 1 (FHM1) mutations in the *Cacna1a* gene. However, the effects of FHM1 mutations on the trigeminovascular system and the release of neuropeptides are largely unknown.

Aim: To investigate the effect in knockin mice with the R192Q mutation on dural vasodilation induced by endogenous and exogenous calcitonin gene-related peptide (CGRP) in a mouse closed cranial window model.

Method: R192Q and wildtype mice were prepared for intravital microscopy on a closed cranial window ($N = 11–16$/group). Vasodilation to endogenous (released by 30 μg/kg capsaicin, iv) or exogenous (10 μg/kg, iv) CGRP was studied by measuring the change in dural artery diameter. This study is approved by the ethics committee of the Erasmus Medical Center in Rotterdam

Results: Baseline dural artery diameter values were comparable in all groups. Capsaicin significantly induced vasodilation in wildtype (88 ± 4 AU vs 40 ± 3 AU) and R192Q (53 ± 6 AU vs 31 ± 4 AU) mice. CGRP induced significant vasodilation in wildtype mice (68 ± 6 AU vs 37 ± 6 AU) and a trend in R192Q mice (46 ± 9 AU vs 34 ± 5 AU). The Δ effects (effect-baseline) induced by capsaicin and CGRP were significantly higher in wildtype (capsaicin: 48 ± 5 AU, CGRP: 31 ± 7 AU) compared with the R192Q (capsaicin: 22 ± 4 AU, CGRP: 11 ± 5 AU) mice.

Conclusion: These results demonstrate that FHM1 mutations when expressed in knockin mice affect CGRP-induced vasodilation in the trigeminovascular system. Thus, FHM1 mutations do not only affect the central aspects of migraine pathophysiology, but also the trigeminovascular components.

PO508

Genetics and biomarkers of headache disorders

Look beyond COMT genotype for cathecolamines derangement in migraine: the biobim rs4818 and rs4680 polymorphisms study

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Background: Catechol-O-Methyltransferase (COMT) is the major enzyme that degrades catecholamines. An impaired catecholaminergic neurotransmission, namely a chronic dopaminergic and noradrenergic hypofunction, is a peculiar migraine trait. This is the first study on COMT rs4818 genotype, the polymorphism most strongly affecting COMT activity. We also provided a replication study on COMT rs4680 polymorphism.

Findings: We performed genotyping of COMT rs4680 and rs4818 gene polymorphisms on 380 carefully clinical characterized migraineurs and 132 healthy subjects matched for age, gender and race-ethnicity, with no clinical evidence or family history of migraine or other neurological diseases. The rs4680 and rs4818 genotypic frequences did not deviate from those expected for a population in Hardy-Weinberg equilibrium and did not correlate with

demographics or clinical migraine features, even when considering migraine subtypes (dopaminergic migraine, menstrual migraine and menstrually related migraine).

Conclusions: COMT genotype does not influence migraine susceptibility or phenotype, even considering rs4818 polymorphism and peculiar migraine clinical subtypes. This finding prompts to look over COMT to explain catecholamine derangement in migraine, exploring enzymes involved in catecholamines synthesis and catabolism such as monoamine-oxidase, dopamine beta hydroxylase, tyrosine hydroxylase or tyrosine decarboxylase.

PO509

Genetics and biomarkers of headache disorders

In vivo and in vitro vascular characterization of a novel transgenic mouse model of migraine

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Background: Migraine is an important cardiovascular risk factor and a prominent feature in Retinal Vasculopathy with Cerebral Leukodystrophy (RVCL), a rare monogenic small vessel disease caused by mutations in *TREX1*, encoding for a 3'-5' DNA exonuclease. It is not known whether TREX1 mutations affect vascular function.

Aim: With a novel knockin transgenic mouse model containing a truncating *TREX1* mutation, we investigated vascular changes in relation to migraine pathogenesis.

Methods: We characterized the *macrovascular* function of these transgenic mice in vitro. Using myographs, relaxations to acetylcholine were measured in isolated aortae. The in vivo *microvascular* characterization was executed by post-occlusive reactive hyperaemia (PORH) measurements of the hindpaw by laser Doppler flowmetry. For both the in vitro and in vivo measurements, we included animals of 13, 26, 52 and 100 weeks of age.

Results: In the in vitro studies, acetylcholine induced lower relaxations in the aortae of the 100 weeks old transgenic (E_{max}:35 ± 7%, n = 8) than in wild type (E_{max}:56 ± 7%, n = 8, p = 0.05) mice. No other differences between wild type and transgenic animals were observed in the in vitro studies. However, in the in vivo experiments, the PORH responses were significantly attenuated in the animals with the *TREX1* mutation across all age groups [$F(1,66) = 5.4$, $p = 0.023$]. Histopathological analyses of RVCL mice retina, skin, kidney and brain are ongoing.

Conclusions: Our analysis is suggestive of vascular abnormalities in this monogenic RVCL model, which may be assigned to decreased endothelial function, especially in the microcirculation. The model is a promising tool to study vascular mechanisms of migraine pathophysiology.

PO510

Genetics and biomarkers of headache disorders

Episodic hypothermia: a migraine equivalent?

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Background: Episodic hypothermia (EH) is characterized by recurrent episodes of hypothermia (<35°C) and profuse sweating without detectable infectious or endocrine cause. It has been proposed EH may be a migraine equivalent. Symptoms are thought to be driven by change in hypothalamic activity, which also occurs during the premonitory phase of a migraine attack.

Methods: We phenotyped a small family with EH.

Results Proband: 3 year-old girl has episodes of hypothermia and cranial hyperhidrosis every 10–14 days. Attacks last 1–2 days and started at age 1.5 years. She is clingy and inactive. Ibuprofen helps somewhat. Sleep helps and often terminates attacks. She's had normal development and is otherwise healthy. General and neurologic examinations are normal.

5 year-old brother: Wakes every 3 months with facial flushing, sweating, fatigue and lethargy. Head feels warm, body feels cool. Symptoms last all day and terminate with sleep. Normal development, normal general and neurologic examinations.

Paternal uncle: In childhood attacks occurred every 2–3 months. Now in his thirties they occur every 6 weeks and last 36 hours. There is a prodrome of sensitivity to touch. Then he awakes with cranial hyperhidrosis, body cool, and fatigue. There is no headache, nausea/vomiting, phonophobia or photophobia.

Whole exome sequencing and genetic analysis of the family is ongoing.

Conclusions: The inheritance pattern appears to be autosomal dominant with incomplete penetrance. The periodicity, relationship to sleep, and hypothermia suggest a hypothalamic localization. Identifying additional affected families could help identify the causative gene/mutation. Understanding EH genetics could help elucidate migraine genetics.

PO511

Genetics and biomarkers of headache disorders

Association of polymorphisms of genes of no synthases and migraine in Moscow

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Background: Nitric oxide (NO) is an important mediator of vasodilation in the intra- and extracranial vessels. This small molecule easily penetrates the membranes of vascular smooth muscle cell, and activates soluble guanylate cyclase and cGMP synthesis, leading to vasodilation. NO also promotes the release of CGRP, which is a powerful vasodilator. The SNPs in genes, coding NO synthases, may influence the pathogenesis of migraine.

The aim of the study was to investigate the prevalence of iNOS (rs2779249), eNOS (rs2070744) and nNOS (rs41279104) polymorphisms of the NOS family genes in migraine patients and controls.

Method: 146 migraine patients (44 with chronic and 96 with episodic migraine, ICHD-III), and 363 unscreened volunteers as the controls (all live in Moscow). SNPs were genotyped by RT-PCR technique using qPCRmix-HS kit (Evrogen) and oligos synthesized by DNA Synthesis, LLC. Reactions were performed in CFX-96 software (BioRad).

Results: Alleles and genotypes frequencies of SNPs in iNOS (rs2779249) and nNOS (rs41279104) were not different in samples of patients and controls. For the SNP in eNOS gene (rs2070744) an association of GG genotype with migraine was found (Chi-square 4.47, $p = 0.03$, OR = 1.88 95%CI = [1.09–3.24], Cochran-Armitage test), the G allele is recessive allele (Chi-square 5.22, $p = 0.02$, OR = 1.88, 95%CI = [1.09–3.24]). When comparing the groups of CM and EM with control the association only with EM was found (Chi-square 4.07, $p = 0.04$, OR = 2.03, 95%CI = [1.09–3.76], Cochran-Armitage test).

Conclusion: The influence of the recessive G allele (rs2070744) of eNOS gene on the pathogenesis of episodic migraine was shown.

PO512

Genetics and biomarkers of headache disorders

Relationship between serum levels of VIP, but not of CGRP, and cranial parasympathetic symptoms: a study in chronic migraine patients

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Background: Cranial parasympathetic autonomic symptoms (CPAS) appear in at least half of migraine patients theoretically as a result of release by an activated trigemino-vascular system of peptides such as VIP.

Objective: To correlate the presence CAPS with serum levels of VIP and CGRP.

Patients and Methods: Patients with chronic migraine (CM) were asked on the presence -during migraine attacks- of 5 CAPS, which were scored by using a quantitative scale (ranging 0–10 points as each symptom could be scored between 0 -absent- and 2 -conspicuous-). Serum VIP and CGRP levels were determined as reported previously by our group (Cernuda-Morollón et al, Neurology 2013; 81: 1191–6 and Cephalalgia 2014; May 20. pii: 0333102414535111).

Results: We interviewed 100 CM patients (93 females; mean age 45 years). Eighteen had no CAPS, while 82 reported at least one CAPS. VIP levels ranged from 20.8 to 668.2 pg/ml (mean = 154.5). There was a significant positive correlation between scores in the CAPS scale and VIP levels (Spearman coefficient = 0.227; $p = 0.035$). VIP levels were significantly higher in CM with at least 1 point in the scale vs those with 0 points ($p = 0.002$). Analysing symptoms individually, VIP levels were

numerically higher in those patients with symptoms, though they were significantly higher only in those patients with lacrimation vs those without it. There was no correlation between CGRP levels and the score in the CAPS scale.

Conclusions: Serum VIP, but not CGRP, levels seem to reflect the rate of activation of the parasympathetic arm of the trigemino-vascular system in migraine.

PO513

Genetics and biomarkers of headache disorders

Congenital ataxia, hemiplegic migraine due to a novel mutation of CACNA1A: a case report

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Background: CACNA1A gene encodes the pore forming alpha-1 A subunit of neuronal voltage-dependent P/Q-type Ca(2+) channels. Mutations in this gene result in clinical heterogeneity, including hemiplegic migraine, episodic ataxia, or progressive chronic conditions.

Case report: a 8 years old boy was admitted to our neurological unit due to an acute onset of left hemiparesis developed after a febrile episode. He complained also headache with migraine characteristics. Brain MRI showed right hemispheric oedema. The hemiparesis disappeared completely after 1 week, and after steroids treatment. The patient was already known to our clinic since he was 2 years old when he was referred to us for a motor and cognitive developmental delay and for a cerebellar syndrome diagnosed as congenital ataxia. In the past all metabolic, biochemical and genetical analysis resulted negative. Serial brain MRI showed a progressive cerebellar atrophy. CACNA1A gene mutation was hypothesised and sequence analysis revealed a heterozygous mutation c.4013C > T (p.I1338T) affecting the S4 segment and potentially damaging to the protein. This is a de novo mutation because it was not found in both parents.

Discussion: to the best our knowledge this mutation of CACNA1A gene has not been reported in the literature. Similar cases of a relatively long history of cerebellar ataxia, cognitive impairment and paroxysmal episodes are reported in the literature due to CACNA1A mutations. CACNA1A mutations present with a wide clinical spectrum. Congenital ataxia, mental retardation, and hemiplegic episode can be the presenting signs of CACNA1A mutations.

PO514

Genetics and biomarkers of headache disorders

Investigation of BDNF and CGRP gene variants in migraine

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Objectives: Migraine pathophysiology involves several pathways. A number of observations have suggested that brain-derived neurotrophic factor (BDNF) and the calcitonin gene-related peptide gene (CGRP) play a role in migraine pathophysiology. Our aim was to explore a role of BDNF single nucleotide polymorphism (SNP) rs2049046 A/T and CGRP SNP rs1553005 C/G in migraine susceptibility and to find possible interaction between them in Russian population.

Method: 144 migraine patients (102 episodic migraine (EM) of which 84 migraine without aura (MO), 18 migraine with aura (MA) and 42 with chronic migraine (CM), ICHD-III), and 202 unscreened volunteers as the controls (all live in Moscow). SNPs were genotyped by PCR-RFPL technique using GenePakTM PCR Core (Isogen Lab Ltd.) and oligos synthesized by DNA Synthesis, LLC. Reactions were performed in T100 software (BioRad). Allelic and haplotypic frequencies were estimated. Intergroup comparisons were made using the Mann-Whitney U test.

Results: BDNF (rs2049046) T-allele was significantly frequent in migraine than in control group (TT $p = 0{,}001$, AT $p = 0{,}004$); in EM group A-allele showed a significant association with MA (AA $p = 0{,}038$, AT $p = 0{,}053$); AA-genotype showed significant association with CGRP rs1553005 (with CC-genotype $p = 0{,}022$, with CG genotype $p = 0.008$). Combination of rs2779249 C-allele and rs2049046 A-allele was significanly higher in migraineurs than in control group ($p = 0{,}012$). Genotypes frequencies of CGRP (rs2779249) were not different in samples of patients and controls.

Conclusion: This study shows that BDNF SNP rs2049046 is associated with migraine susceptibility.

Also our data supports the previous studies of interaction between BDNF and CGRP in migraine.

PO515

Genetics and biomarkers of headache disorders

A novel PRRT2 mutation in a patient with familial hemiplegic migraine

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Background: Familial hemiplegic migraine (FHM) has been classically associated with mutations in CACNA1A, ATP1A2 and SCN1A genes. Recent reports suggest that the proline-rich transmembrane protein (PRRT2) gene might play a role in the development of FHM. PRRT2 gene mutations have been associated with paroxysmal kinesigenic dyskinesia, benign familial infantile seizures, or infantile convulsion choreoathetosis syndrome.

Aim: To describe a novel mutation in PRRT2 in a patient fulfilling criteria for FHM (ICHD-III).

Methods: 34-year-old Caucasian woman with a 24-year history of headache with aura including motor weakness. Episodes began with visual impairment on right field followed with sensory disturbance and motor weakness spreading from right limbs to ipsilateral face. This entire picture was fully reversible in two hours and was followed by a moderate pulsating frontal pain accompanied by nausea and photophobia. No abnormalities in brain neuroimaging. Attacks recurred twice a year. She described similar episodes in her father and grandmother. No other familial neurologic syndromes.

Results: Genomic DNA was extracted from peripheral blood and exons were amplified using PCR primers. Capture and massive sequencing of human exome was carried out by using SureSelect Human All Exon 51 Mb kit (Agilent) assay and Hiseq2000 (Illumina) 30x tests. Candidate genes data were analyzed and compared with hg19 version of the human genome. We identified an undescribed variant in heterozygous state in PRRT2 gene (c.641delC:p.A214fs), pathogenic according to different prediction algorithms.

Conclusion: More studies are needed to support the specific role of the PRRT2 gene in FHM and its coexistence with other channelopathies.

PO516

Genetics and biomarkers of headache disorders

Association of angiotensin-converting enzyme (ACE) gene (insertion/deletion) polymorphism (rs4646994) with migraine

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Background: The relationship between genetic polymorphisms, migraine and endothelial dysfunction are physiologically convincing but remain controversial.

Aim: The present study was aimed to investigate the relationship between ACE polymorphism (rs 4646994) and migraine (both with and without aura).

Methods:137 migraine patients aged 18–65 (112 migraine without aura (MoA), 25 migraine with aura (MwA)) and 153 age- and gender-matched healthy controls were included in the study. We investigated associations between ACE insertion/deletion (I/D) polymorphism and clinical features of migraineurs.

Results: Genotypic frequencies: ACE DD 28%, ID 46%, II 26% forMoA group, DD 6%, ID 44%, II 50% for MwA group and DD 35%, ID 40%, II 25% in the control group. The significant association was found between ACE I/I polymorphism and migraine aura($p < 0.02$).

Conclusions: Our data suggested that ACE polymorphism (rs 4646994) may play a role in migraine with aura susceptibility in Russian population. Data from this study confirmed a possible relationship between ACE activity, migraine aura and endothelial dysfunction.

PO517

Genetics and biomarkers of headache disorders

Complex genetic analysis for migraine by CACNAIA gene analysis

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Background: Familial hemiplegic migraine type 1 (FHM1) is a form of migraine with aura characterized by recurrent attacks of migraine headache with transient hemiparesis during the aura phase. FHM is caused by heterozygous mutations in 4 genes: *CACNA1A*, *ATP1A2*, *SNC1A* and *PRRT2*, but further heterogeneity is expected.

Aims: To describe clinical and molecular features in patients suffering from MA, MO and hemiplegic migraine attacks.

Methods: Next Generation Sequencing by TruSeq Custom Amplicon for CACNA1A and ATP1A2 gene has been performed. All genetic variants have been confirmed by Sanger sequencing and all samples were also analyzed with MLPA assay for ATP1A2-CACNA1A genes to detect duplication or deletion. All MLPA data were verified by Real Time PCR.

Results: 37 patients with FHM/SHM have been analysed: 35 resulted negative for sequencing analysis and a point mutation has been detected in 2 consanguineous patients (brothers). The same samples have been analysed by MLPA finding 3 deletions (8.1%). 72 individuals with MA/MO have been studied and 4 deletions have been found. Microsatellites analysis regarding the repetitive sequence (CAG)n in the 3' untranslated region of the 47 exon of the gene of interest has been carried out.

Discussion: This work highlights the importance to complement analysis as direct sequencing with quantitative analysis (MLPA). In fact**,** intragenic CACNA1A rearrangements have been detected. The deleted allele is predicted to lead a truncated protein or to absence of the protein caused by mRNA instability. Interesting, in all patients, *CACNA1A* deletions are associated with an early disease onset.

PO519

Psychological and behavioral factors and management

Mental health in relation to prevalence of headache in Nepal: results from a nationwide population based study

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Background: Western studies have shown associations between headache, anxiety and depression, but such links in the general populations of South Asian countries are not yet scientifically proven.

Aim: To look for associations of anxiety, depression and neuroticism with headache prevalence (1-year and/or 1-day [headache yesterday]) in Nepal, a South Asian country.

Methods: In a nationwide, cross-sectional survey of the adult Nepali population (N = 2,100), trained interviewers applied: 1) a culturally-adapted version of the *Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation* (HARDSHIP) questionnaire to detect any headache in the last year (and assess its frequency) and yesterday; 2) validated Nepali versions of the *Hospital Anxiety Depression Scale* (HADS) and *Eysenck Personality Questionnaire-Neuroticism* (EPQ-N). Informed consent was obtained according to the requirements of the review boards for research ethics in Nepal and Norway. Logistic regression analysis was used in three blocks: socio-demographic variables, substances use and mental health.

Results: Anxiety was significantly associated with headache in the last year (OR 1.1, 95% CI 1.05–1.16), headache occurring on ≥15 days/month (OR 1.1, 95%CI 1.07–1.2) and headache yesterday (OR 1.1, 95% CI 1.05–1.15), while neither depression nor neuroticism reached significance in the multivariate analyses. Alcohol use (yes/no), as a covariate, was significantly associated with 1-year prevalence (OR 1.76, 95% CI 1.32–2.36).

Conclusion: The association between anxiety and headache was not very strong, but significant, independent and constant. This finding indicates that there may be a universal psychiatric link to headache independent of culture. This is an important finding, requiring and calling for further exploration.

PO520

Psychological and behavioral factors and management

Relationship between a history of sexual abuse in chronic migraineurs versus episodic migraineurs

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Background - Sexual abuse is a widespread problem that has been associated with the development of psychological and physical conditions. Migraineurs often have a history of physical, emotional, and sexual abuse.

Aim - To assess rates of reported sexual abuse history in chronic migraineurs versus episodic migraineurs.

Method: A retrospective chart review was conducted utilizing the medical records of all new patients at a headache clinic during a four-month period. New patient questionnaires, which included a field for history of sexual abuse, were assessed. All new patients with a diagnosis of chronic migraine, and migraine with or without aura, were included. IRB waived the need for informed consent.

Result: A total of 329 migraineurs were included in the review. Chronic migraine diagnosis was recorded in 194 patients, and episodic migraine diagnosis was recorded in 135 patients. Of the chronic migraine patients, 20 reported a history of sexual abuse (15.5%), whereas 5 episodic migraine patients reported a history of sexual abuse (4.4%). Chi-square indicated that patients with chronic migraine are significantly more likely to report a sexual abuse history, compared to patients with episodic migraine.

Conclusion: These findings suggest that a history of sexual abuse can be a factor in the transformation of episodic migraine to chronic migraine. The study underscores the importance of intervention, such as psychotherapy, in patients who have suffered such abuse. It also highlights the importance of aggressive treatment of episodic migraine in patients with a history of sexual abuse, in order to help prevent transformation to chronic migraine.

PO521

Psychological and behavioral factors and management

Issues in our understanding and management of the triggers of headache and migraine

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Recent years have seen an upsurge of interest in the triggers of headache and migraine. Hence it is timely to consider the myriad of issues in this domain.

1. **Conceptual issues** – there are definitional issues as the typical list of triggers includes triggers specified as: stimuli, responses, transactions between stimuli and responses, and presumed mechanisms. There are issues pertaining to trigger potency/dosage and sensitivity/susceptibility to triggers.

2. C**omplexity issues** – triggers may precipitate headaches in isolation, or may aggregate to cause headaches, or may only precipitate headaches in certain psychosocial/developmental contexts. Triggers may precipitate headaches but then the reaction to the headache augments the trigger.

3. **Aetiological issues** – how does a trigger acquire and lose the capacity to precipitate headaches?

4. **Empirical issues** – the evidence available in support of the capacity of triggers to precipitate headaches is variable, and not completely convincing for any trigger.

5. **Methodological issues** – it is very difficult to demonstrate whether a perceived trigger is a trigger either at the clinical/individual level or the research/group level.

6. **Mechanism issues** – do triggers precipitate headaches via a common neurobiological mechanism or multiple pathways?

7. **Clinical issues** – for many decades the standard advice to headache sufferers is that they should try to avoid the triggers, but this advice has been challenged in recent years, with exposure advocated for some triggers on the basis of trigger desensitisation.

The presenter has been conducting research on headache triggers for over 20 years, and will discuss ways forward.

PO523

Psychological and behavioral factors and management

Perspecrive of patients with migraine

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Migraine is a chronic neurological condition with heterogeneous clinical presentations. It can cause a limitation of dayly activities. Same patitents expect to find abnormalities in imagingstudies to explainthe problem or have concerns related to diagnosis and treatment. Others are unaware that their lifestyle can influence the frecuency of headache. Preventive treatmens require prolonged administration of medications with possible side effects.

Aim: To determine the patients perspective regarding migraine.

Methods: 12 question survey was administered to our migrained patients.

Result: 100 patients were interviewed. Age range:21–62, 97.3% understood the diagnosis, 44% of patient reported the their inquiry hade not been valued by other doctors. 98% believe that migraine impairs their quality of live and 40% peferred an abnormal brain RMN an as explanation. 61% believed that the daily habits influence their headaches and 83% recagniced the importance of headache diary, The major concern was the limitations of migraine on daily activities 35%, folllowed by the change of mood 27%, health risk 21%, and medications 17%.

With preventative medications: 62% felt safe and 24% felt fear, 31% didn't take the symptomatic medication inmediately. 83% knew that the high use analgesics may aggravate the headache.

Conclusion: Migraine significantly compromises the quality of life. However, the migraine diagnosis remains undervaluated in medical practice.

It is important to explaint the neurobiological origin and provide preventive treatment in cases that require it understanding the concerns and reducing patient fears regarding the use of prophylaxis could improve their adherence to treatment.

PO524

Psychological and behavioral factors and management

Cognitive and personality traits in medication overuse headache

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Background: Psychopathology, personality and cognitive factors might play a role in Medication Overuse Headache (MOH). Self-efficacy, strength of one's belief in one's own ability to complete tasks and reach goals, has been linked to behavioral aspects such as therapeutic adherence and medication use control.

Aim: Purpose of this study is obtaining information about psycho-social aspects (anxiety level; depression levels; psychopathological comorbidity; personality traits; self-efficacy; disability) of MOH patients referred to our headache center.

Method: Clinical and psycho-social information from records of 76 confirmed MOH patients (12 males; 65 females) from 20 to 71 years old aged (M: 38.05; DS: 8.01) accessing our center from January 2014 to December 2014 were retrieved; Personality and psychopatology (DSM-IV-TR interview), anxiety and depression (Zung questionnaires), disability (MIDAS questionnaire), medication use and self-efficacy (Hart questionnaire) were assessed. Frequencies and covariance analyses were performed to evaluate the correlation between headache frequency, medication use, anxiety, depression, disability.

Results: Psychopathological comorbidities (61.76%) are mood (30.80%), anxiety, (20.57%) and personality disorders (10.39%); Mean anxiety and depression levels are middle-to-high (Zung-A $M = 49.14$; Zung-D $M = 55.53$); Prevalent personality traits are: evitating (29.98%), obsessive-compulsive (25.52%) and dependent (19.75%); self-efficacy is middle-to-low (82%); disability is high (MIDAS $M = 43.42$); migraine frequency directly correlates with anxiety ($p < 0.01$), depression ($p < 0.05$), overuse ($p < 0.05$) and disability level ($p < 0.05$). Medication overuse positively correlates with disability ($p < 0.05$);

Conclusions: Data suggest that anxious cluster personality traits and cognitive features such a weak self-efficacy might contribute to MOH and related behaviors.

PO525

Psychological and behavioral factors and management

Neuropsychological profiling and cognitive impairment in a case of chronic migraine with probable medication overuse headache

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Background: neuropsychological features are believed related to Chronic Migraine (CM) and Medication Overuse Headache (MOH). Data about this relationship are conflicting.

Aim: we assessed the neuropsychological functioning of a CM with probable MOH patient showing cognitive issues at a psychological interview, to investigate a neuropsychological profile related to the headache.

Method: we present the open study of a case of a 52 years old woman with a 15 years long history of CM and pMOH, currently in clinical observation. MRI showed occipital arachnoid cyst. VMRA was negative. At a psychological evaluation attention issues, memory loss and anxious personality traits were detected. Psychometric scores were normal but mild impulsiveness was measured. MIDAS showed high level of disability. A neuropsychological assessment consisting of tests regarding general cognitive efficiency, memory and constructional praxis was performed.

Results: the neuropsychological profile was normal regarding: verbal memory; constructional praxis; selective attention; strategic planning; it was borderline regarding: general cognitive efficiency; abstract logical reasoning; prose memory; semantic fluency; spatial planning and attention; deficits were detected regarding: visual short term memory; verbal long term memory; visual long term memory; phonemic fluency.

Conclusions: the neuropsychological impairments (impulse control, decision making and problem solving) could be related with behavioral aspects relevant to CM and MOH such as non-adherence and compulsive medication use. Deficits could be related to malfunctioning frontal processes, like attention, selection and retrieval of information.

PO526

Psychological and behavioral factors and management

Combined cognitive-behavioral and pharmacological therapies for chronic migraine and chronic tension-type headache: are treatment responses different?

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Background: According to international guidelines cognitive-behavioral therapy (CBT) is of value in migraine (M) prevention. Combination of pharmacological therapy and CBT is superior to single therapies for M and TTH. If combined treatment has less or comparable efficacy in TTH and M is still discussed.

Aim: To compare treatment responses to pharmacotherapy and CBT in patients with CM and CTTH.

Methods: the study included 62 patients with CDH aged 23–78 years (m. age = 47,19 ± 11,79) who were assigned to three groups: 1) CM (N = 21;33,87% patients); 2) CTTH and episodic migraine (EM) (N = 15;24,19%); 3) CTTH (N = 26;41,94%). All patients received combination of adequate pharmacotherapy and CBT. Patients with MOH underwent withdrawal therapy. Prospective analysis of clinical-psychological characteristics was performed before treatment, at the end of 3 and 6 months of treatment.

Results: The three study groups were comparable in terms of socio-demographic characteristics**,** disease duration, psychometric parameters at baseline (levels of depression, anxiety, personality disorders, pain catastrophizing), prevalence of MOH, types of psychiatric disorders and fibromyalgia. At 6th month of treatment 66,13% (N = 41) of all patients experienced at least 50% reduction of headache days. The number of responders didn't differ significantly between groups ($p > 0.05$). Significant positive correlations were revealed between the presence of pericranial myofacial pain syndrome (PMPS) and treatment responses in CTTH with and without EM ($p < 0,05$).

Conclusion: Combined CBT and pharmacotherapy have similar effectiveness in CM and CTTH with or without EM. PMPS is predictive factor of treatment response only in CTTH with or without EM but not in CM.

PO527

Psychological and behavioral factors and management

Analysis of voice within patients with migraine headaches

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Background: The aim of this study was to investigate the effect of migraine headaches on the acoustic characteristics of voice in patients during and after migraine attacks.

Methods: The study included 32 subjects aged 37–58 years. The study subjects was recorded voice during migraine headaches and 10 days after a migraine headaches. Analysis of the acoustic parameters of the voice was evaluated by analyzing acoustic parameters of voice, using "Multi−dimensional Voice Program" of computerized laboratory "Key Elemetrics". The research was carried out individually while the subject was seated in a quiet room. Microphone was placed at 5 cm distance from the patient's mouth. For credibility of the results, each group repeated the sustained vowel /a/ at their habitual pitch and loudness level for at least 3 s durations, three times, of which, the one with mean value was considered relevant for the analysis. The data were analyzed by descriptive statistics and analytical statistics: Student's t-test for dependent samples, Hi-square $\chi 2$ test, Man Whitney U-test and Pearson's rank correlation coefficient – ρ.

Results: The results showed that statistically significant differences in mean values of the examined parameters of voice occur as a consequence of migraine attacks ($p < 0.01$), while the sex, age and smoking status did not have a significant impact on the acoustic characteristics of voice in our patients ($p > 0.05$).

Keywords: Migraine headaches, Voice, Acoustic characteristics of voice

PO528

Psychological and behavioral factors and management

Cost-effectiveness of self-management education versus usual care for patients with migraine headache: a pilot randomized controlled trial

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Background: Headache is one of the common health conditions affecting society. In the context of high costs to patients, the health care system and society, the need for providing cost-effective care is apparent.

Aim: To estimate the service and social costs of people with headache, and to compare the cost-effectiveness of participants randomised to receive minimal contact cognitive behaviour therapy (CBT) and relaxation with those receiving standard medical care (SMC) alone.

Method: Participants recruited from specialist headache clinics across London were randomised to receive CBT and relaxation (plus SMC) or SMC alone. Service use over a four month period before and after randomisation was measured and lost employment recorded. These data were used to estimate economic costs. Predictors of cost were identified using regression and cost-effectiveness was compared by combining the costs with QALYs.

Results: The mean service and total costs were £858 and £6588 respectively. Service costs were significantly related to the number of days spent with headache and total costs were significantly related to the impact of headache. In the cost-effectiveness analysis, the ICER was £39,492 from the health care perspective. From the societal perspective, the intervention was dominant with 55.2% chance that it will results in lower costs and better outcomes at cost-effectiveness threshold of £20000 per QALY.

Conclusion: Costs of headache are high and associated with severity. The intervention was not cost-effective from a healthcare perspective but was from a societal one.

PO529

Psychological and behavioral factors and management

Behavioural treatments for migraine headache: the patients' view

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Background: The National Institute of Clinical Excellence (NICE) recommends evidence is needed of the effect of psychological interventions, like cognitive behaviour therapy, for chronic headache disorders in the NHS context. We found little evidence from mixed methods trials, including qualitative research, and undertook a pilot mixed-methods trial of minimal contact behavioural treatment (relaxation and CBT).

Aim: We aimed to examine patients' experience and responses to behavioural treatment to inform a full-scale trial and its translation into clinical practice.

Method: We conducted a pilot trial, with a nested qualitative study in London. Twenty participants who had received the minimal contact relaxation and CBT treatment took part. Semi-structured Interviews were recorded and transcribed. Transcripts were coded to a thematic framework developed according to the topic guide. Theme data was then extracted and summarised.

Results: The majority of participants cited their desire for additional non-drug treatment as a main reason for taking part. Overall the majority of participants reported benefiting from treatment, either through a direct effect on their headache management or from daily stress reduction. Relaxation training (deep breathing), were easily adopted. CBT was more challenging to learn and implement.

Conclusion: Relaxation training is deliverable and easily implemented. CBT for migraine may require longer than a minimal contact intervention to be applied successful by patients in the UK NHS context.

PO530

Psychological and behavioral factors and management

Do ayurvedic constitution types influence the quality of life of headache patients?

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Background: According to Ayurveda, every individual has a combination of 3 major constitution types, affecting the state of health and disease. According to previous observations, these constitution types show a number of biochemical, haematological, and genetic differences. Some of these constitution types may have a positive effect on headache related quality of life as well.

Aim: To examine the possible effect of Ayurveda constitution types on headache-related quality of life.

Method: A pilot study was conducted on 35 individuals (age: 36.4 ± 10.4; 25 females) suffering from Migraine ($N = 13$), Tension type headache ($N = 7$) or Unspecified headache ($N = 15$). Constitution types were determined according to Ayurveda principles using the Prakriti Analysis Inventory. Quality of life was measured by the CHQQ instrument. The data were analyzed using t-tests.

Results: In this study, out of 35 people, 31 individuals (88.57%) had Pitta as one of the major body constitutions. Individuals with Kapha Pitta and Pitta Kapha constitution types had higher CHQQ scores than individuals with other constitution types ($p = 0.039$). Migraineurs with the Kapha Pitta and Pitta Kapha constitution types also had numerically higher CHQQ scores than migraineurs with other constitution types ($p = 0.062$).

Conclusion: This pilot study supports the concept of Ayurveda that the tolerance to headaches, and probably to migraines is better in Kapha and Pitta individuals as demonstrated by higher CHQQ scores. This study also raises the possibility that Ayurveda constitution types can influence quality of life in different headache types. Further studies with a higher number of patients may substantiate this notion.

PO531

Psychological and behavioral factors and management

Babinski's lost legacy

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- Background/aim: To report a remarkable case of migraine with brainstem aura (MBA) accompanied by conversion disorder (CD) and non-epileptic psychogenic seizures (NEPS).
- Method: A 45-year-old woman, with migrainous family and medical history of pharmacorefractory epileptic seizures in adolescence, consulted for a daytime 1 year-course clinical picture, facilitated by emotional stress, of daily 30–40 minutes long self-limited episodes, characterized by generalized paraesthesia, binocular diplopia, dysarthria, and "seizures" (like those suffered as a teenager), with immediate consciousness recovery, and later, occipito-pulsatile headache.
- Results: Neurological examination after suggestion highlighted: obtundation, mutism, closed eyes (with opening resistance), axial-appendicular paroxystic and changing pseudodystonias with asynchronous pelvic contortion and kicking, combined with flexo-extension generalized movements, and transient opisthotonos. Blood test, ECG, Holter-ECG, neuroimaging, EEG, and video-EEG were normal. After psychiatric evaluation, diagnosis of MBA with CD and NEPS was made. Finally, antimigrainous prophylactic treatment, anxiolytic medication, and psychotherapy achieved significant patient's clinical improvement.
- Conclusion: Psychiatric disorders during migraine attacks are not uncommon. In 1890 Babinski described as *migraine ophthalmique hystérique*, four migraine cases with visual aura and hysteria. Ignorance of this nosological entity is motivated by the arduous historical task that represents to define CD. However, migraine associated with CD, or Babinski's migraine (BM), is a well-documented migrainous subtype which requires an interdisciplinary approach by Neurology, Psychiatry, and Psychology. In conclusion, we propose to include BM as diagnostic subcategory within MBA, in order to rescue this Babinski's legacy, omitted for decades, seeking to achieve better diagnostic approach and optimal therapy application that improve patients' life quality.

PO534

Psychological and behavioral factors and management

Neuropsychological assessment in patients with chronic migraine with overuse headache, episodic migraine and controls

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Background: Medication-overuse headache is a chronic disorder defined as induced by the overuse of acute headache compounds. Orbitofrontal cortex dysfunction and poor decision making have been described in chronic migraine with medication overuse, as dorsolateral cortex dysfunction both in chronic migraine with medication overuse and episodic migraine.

Aim: The aim of this study was to evaluate orbitofrontal and dorsolateral dysfunction in patients with chronic migraine with overuse headache, episodic migraine and controls.

Method: A cross-sectional and prospective study including 30 adult patients (10 patients with chronic migraine and medication overuse, 10 episodic migraineurs and 10 controls) evaluated between January and December 2014 in Irmandade Santa Casa de Misericórdia de Porto Alegre/Brazil. All individuals were interviewed by neurologist to establish headache diagnosis according to the ICHD-3 beta criteria and submitted to a battery of neuropsychological tasks evaluating the orbitofrontal and dorsolateral functioning. Depression and anxiety evaluation were also performed. This study was approved by the research ethics committee of the hospital (protocol number 471268) and all patients gave written informed consent.

Results: Chronic migraineurs with medication overuse headache showed a significant impairment in dorsolateral task performance as to compare to episodic migraineurs and controls. No difference was found on depression and anxiety scores and orbitofrontal task performance between the groups.

Conclusion: Neuropsychological evaluation in migraine may be helpful to indicate patients prone to overuse.

Further investigations would be important to elucidate this subject.

PO535

Psychological and behavioral factors and management

Childhood headache features and psychological symptoms: the role of attachment style

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Background: Attachment theory suggests that early interpersonal relationships may be important determinants of psychopathology and pain management. Few studies focused on headache and data on attachment style in pediatric headache are scarce.

Aim: To investigate the relationship between the clinical features of headache (intensity and/or frequency) and the psychological symptoms in patients with different attachment styles.

Methods: We studied 78 children/adolescents with migraine (boys = 35; girls = 43). Patients were divided according to the migraine severity (mild/moderate and severe) and frequency (high and low). The psychological profile was assessed by SAFA Anxiety, Depression and Somatization scales. Attachment style was measured by the semi-projective test Separation Anxiety Test. Children were divided into 'secure'', 'avoidant'', 'ambivalent'' and 'disorganized/confused'' attachment patterns.

Results: Due to their low frequencies, the 'disorganized'' and the 'secure'' attachment categories were eliminated from analysis. Most patients (57.7%) showed an 'ambivalent'' attachment style, while 42.3% patients were classified as 'avoiding'' style. Compared to the 'avoiding'', the 'ambivalent'' group had higher anxiety level (SAFA Total: $p = 0.002$). When we analyzed the SAFA scales as function of intensity and/or frequency of attacks according to the two attachment styles, the 'low self esteem'' and 'regret'' subscales (SAFA Depression) showed a relationship with the intensity of pain in avoiding group2.

Conclusions: Our results suggest a relationship between insecure attachment style and headache in children. We can hypothesize that assigning more importance to performances, children classified as 'avoiding'' tend to experience low self esteem and regret if the intensity of pain adversely affects their activity.

PO536

Psychological and behavioral factors and management

Maternal attachment style and alexithymia: is there a relationship with their children headache feature and psychological profile?

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Background: There is evidence that caregivers' attachment styles and the way of management/expression of emotions (alexithymia traits) may influence children's psychological profile and pain expression. However, data dealing with headache are scarce.

Aim: To investigate the role of maternal attachment style and alexithymia ontheir children headache feature (intensity and frequency) and psychological profile (anxiety, depression, somatization).

Methods: Eighty-four children/adolescents with primary headache (mean age 11.5; s.d. 2.4) and their mother were included. Patients were divided according to the headache severityand frequency. The psychological profile was assessed by SAFA Anxiety, Depression and Somatization scales. Attachment style was measured by the semi-projective test SAT. We used ASQ and TAS-20 questionnaires to assess respectively the maternal attachment style and alexithymia levels.

Results: TAS-20 subscale ''Difficulty Describing Feelings'' showed a significant higher scores in mothers whose children reported a ''high'' attacks frequency compared to those whose children complained a ''low'' frequency ($p = 0.007$). No differences was found according the intensity of pain ($p = 0.08$) A positive significant relationship between TAS-20 and SAFA-Anxiety total scores was found ($p = 0.028$). Moreover, we found a significant higher score in maternal alexithymia levels in children classified as ''ambivalent'', compared to those classified as ''avoiding''(Total scale: $p = 0.002$). No differences were found between groups in ASQ subscales.

Conclusions: We can hypothesize that mothers' difficulty in expression and management of emotions increase their children anxiety levels; on the other hand, children may express their distress through recurrent headache in order to be comforted by their mothers.

PO537

Psychological and behavioral factors and management

Migraine equivalents, psychological symptoms and headache features: which relationship?

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Background: Migraine equivalents are common clinical conditions in children suffering from headache. Very few studies dealt with the psychological profile of children/adolescents with migraine equivalents.

Aim: We compared the psychological profile between migraineurs children with and without migraine equivalents; moreover, we explored the role of psychological factors on the intensity and frequency of pediatric migraine attacks.

Methods: We enrolled 136 young migraineurs. They were divided in two groups (patients with and without migraine equivalents). Patients were divided into two groups according to the attack frequency (low and high frequency). Pain intensity was rated on a 3-levels graduate scale (mild, moderate and severe pain). The psychological profile was assessed by means of SAFA Anxiety and Somatization questionnaires.

Results: Migraine equivalents were present in 101 patients (74.3%). They showed higher scores in anxiety (SAFA-A Tot: $p = 0.024$) and somatization (SAFA-S Tot: $p = 0.001$) symptoms, but not in hypochondria levels ($p = 0.26$). In children with migraine equivalents, a low frequency of attacks was related to separation anxiety ($p = 0.034$).

Conclusions: Migraine equivalents patients tend to feel more fearful and to experience more shyness. This, together with the somatization tendency, may lead them to become vigilant in attachment relationships with their caregivers.

PO538

Psychological and behavioral factors and management

Placebo effect of aesthetic packaging design in treatment of headaches

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Introduction: Packaging is an extrinsic part of the product. Many studies examine the influence of packaging design on consumer behavior. Our study tests the influence of pharmaceutical packaging design on preference and satisfaction.

Methods: The effect of aesthetic packaging design of two brands of analgesic used to treat headaches was studied in a sample of women and men when they suffer from headaches. We first conducted a pretest to identify two brand's packaging: the most attractive and the least attractive. The two brands of analgesic contain an active formulation. The sample was randomly into two groups in which subjects received the brand to have an attractive packaging design (Group 1), or that which is have an unattractive packaging design (Group 2). Data were collected by the subjects themselves when they suffered from headaches through a numerical scale of pain assessment. Subjects evaluated their pain before taking an effervescent tablet 500 mg, then 20 min, 2 h and 4 h after taking it.

Results: The two groups have respectively at the evaluation times $t0 = 5{,}96$; $t1 = 3{,}83$; $t2 = 2{,}38$; $t3 = 1{,}85$ for the Group 1and $t0 = 5{,}86$; $t1 = 4{,}3$; $t2 = 2{,}19$; $t3 = 1{,}05$ for the Group 2.

We found no significant differences ($p > 0{,}05$, $p = 0{,}736$) between the potency of the attractive brand packaging analgesic and the unattractive one.

Conclusion: The findings showed that pharmaceutical packaging has no additional marketing placebo effect. Our results suggest that an attractive brand of analgesic has the same potency than an unattractive brand in relieving headaches.

PO539

Psychological and behavioral factors and management

Pain catastrophizing in chronic migraine: results in a series of 28 patients

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Background: Pain Catastrophizing (PC), defined as persistent negative cognitive and emotional responses to pain, is considered among factors that contribute to pain chronicity.

Aim: Assess PC in a series of Chronic Migraine (CM) patients, and its association with mood disorders or headache severity.

Methods: CM patients consecutively attended in a Headache Unit. They answered Hospital Anxiety and Depression Scale (HADS). Headache impact was measured administering six-item Headache Impact Test (HIT-6). PC was assessed with Pain Catastrophizing Scale (PCS). In PCS, patients are asked to indicate the degree they experienced 13 thoughts or feelings when suffering pain, on 5-point scales with end points 0-not at all and 4-all the time. PCS score over 30 is considered clinically relevant catastrophizing.

Results: 28 patients (22 females, 6 males). Age at inclusion 40.7 ± 11 years (20–57) and latency from CM onset 47.3 ± 65.1 months (3–300). Mean HIT-6 score was 62.8 ± 6 (46–74); in 21 patients (75%) severe headache-related impact (HIT-6 ≥ 60). Scores of 7.2 ± 4 (1–17) in HADS-Anxiety and 2.6 ± 3 (0–12) in HADS-Depression. Five (17.9%) cases met criteria for anxiety and 1 (3.6%) for depression. Score of 20.3 ± 11.4 (5–42) in PCS and in 8 patients (28.6%) clinically relevant PC. We found no differences in HADS o HIT-6 scores, and presence of severe headache-impact, anxiety or depression when comparing groups with or without clinically relevant PC.

Conclusion: Catastrophizing is common among CM patients. Correlation with headache impact or mood disorders should be assessed on larger series.

PO540

Psychological and behavioral factors and management

Population-based non-pharmacological intervention for primary headaches prevention

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Primary headaches affect a substantial proportion of individuals' quality of life in general population. Standard treatment includes acute and preventive strategies, guidelines suggest non-pharmacological and pharmacological options, limited population-based interventions are available.

We screened a population of 790 individuals in a poor population, urban/rural area in Novo Airão, Amazon, Brazil, 559 have had headaches in the past year. Seventy-four patients (9,3% of population) with migraine or tension-type were invited to the treatment program due to their severity (MIDAS grade IV). Three interventions were offered, patients were enrolled in 1. Physical activity program (PA), 2. Behavioral intervention (BE), or 3. Physical and Behavioral combined intervention (PA + BE). Local health agents were involved and received training to monitor compliance. No pharmacological prophylaxis was available due to limited local resources. Fifty-seven patients (9 men, 48 women) were enrolled and completed the study. The groups BE($n = 24$), PA($n = 18$), and PA + BE ($n = 15$) matched on age, sex, BMI, education, and headaches subtypes at baseline. All patients signed informed consent, national IRB system approved the protocol. After 6 months all groups improved significantly in number of headache days, duration, intensity, disability, comparing to baseline measures ($p < 0.0000$), but no difference was found between groups. Exercise level measured by IPAQ increased in PA($p = 0.012$) and PA + BE($p = 0.02$), but not in BE group. No difference in compliance was found between groups, but adherence was significantly correlated with headache outcome, more importantly in the combine BE + PA group. This population-based non-pharmacological preventive program is effective, other programs should be planned integrating pharmacotherapy.

PO541

Psychological and behavioral factors and management

Emdr-therapie can reduce stress accompanying a migraine-attack and affects daily functioning positive

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Objectives: This case-report shows the influence of EMDR-therapy on anxious arousal and thoughts accompanying migraine attacks.

Background: Stress is one off the greatest psychological factors that influences a migraine attack. EMDR (Eye Movement Desensitization and Reprocessing) is a therapeutic technic to reduce distress after a trauma and stress-related memory's.1. Sometimes there are traumatic incidents in the history which arouses the stress level. 2. Every migraine-attack could be seen as a traumatic experience with emotional aspects and disfunctional thoughts. 3. Finally fear for the next migraine-attack results in more arousal and can facilitate an attack. The hypothesis is that a treatment with EMDR influences the pain-networks in the brain and the disfunctional pain-information.

Methods: a case report. A-self report questionnaire before and after treatment was taken. A EMDR-procedure for negative emotions and stress was used for treatment.

Results: A 35 year old woman with chronic migraine during pregnancy and high frequency migraine before and after pregnancy. She was anxious for the sudden aura's and disfunctional periods afterwards. Her history showed several migraine attacks with distress and negative traumatic memory's about the pain. The treatment with EMDR in 6 sessions over a period of 12 weeks had a positive effect on stress and her anxious level for aura's. Daily functioning improved.

Conclusions: The result suggests that EMDR-therapy in a patient with distress and anxiousness around a migraine-attack provides a benefit by stressreduction and better coping with migraine attacks.

PO542

Psychological and behavioral factors and management

Optimism and pessimism in migraine patients

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Migraine is often associated with psychological aspects and comorbid with psychiatric disorders, but the underlying mechanisms are poorly understood. Optimism and pessimism are positive psychology constructs studied in several mental and brain disorders. They have been implicated as independent psychosocial determinants of pain experience, and also predictors for placebo response in clinical trials. Very little information is available about optimism and pessimism in migraine patients. We studied 362 migraine sufferers who filled IHS diagnostic criteria, 65 chronic, 297 episodic, compared to 150 controls without headache. Patients filled out the Life Orientation Test – revised, the standard questionnaire used to assess optimism and pessimism. Optimism scores were higher in controls compared to migraine patients ($12.2 +- 2.3$ vs $11.6 +- 2.5$; $p < 0,05$), but chronic migraineurs were not different from episodics. Pessimism scores were significantly lower in controls compared to migraine patients ($8.0 +- 2.7$ vs $6.5 +- 2.6$; $p < 0,0001$). No differences comparing chronics versus episodic migraine patients regarding pessimism scores. The difference found in pessimism scores are more pronounced than the observed in optimism. A more negative expectation and / or a less positive expectation seen in this study may be independent underlying mechanisms in migraine or could be related to anxiety and depression, frequently comorbid with migraine. Response to migraine treatment could also be mediated by optimism and pessimism since they are already known to be important factors in placebo response. Optimism and pessimism should be taken into account in assessing migraine patients with implications into pathophysiology and treatment.

PO543

Psychological and behavioral factors and management

In irritable bowel syndrome, a high prevalence of migraine characterizes the subgroup of patients with meal-induced abdominal distention

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Background and Aim: Migraine is a frequent symptom in patients suffering from functional gastrointestinal disorders. We have already shown that in patients with severe postprandial abdominal distention this bothersome symptom occurs in a strict temporal association with a pathologic reduction of recto-sigmoid tone and with the physiologic meal-related gastric accommodation reflex. Since this latter reflex is under nitrergic control, we analyzed the prevalence of migraine in the group of patients with IBS and severe post-prandial abdominal distention in comparison with the subgroup of patients with IBS without post-prandial abdominal distention.

Patients and Methods: One hundred and twenty-four IBS patients (84 F, mean age 31 $\pm$ 6 yrs) diagnosed according to ROME III criteria, were enrolled. In 44 patients a constipated IBS was present, in 66 a diarrhoic IBS and in 14 a mixed IBS. In all, an accurate definition of the presence of migraine without aura was analyzed, according to ICHD-III beta version criteria.

Results: Among the 124 enrolled patients, 60 suffered from severe postprandial abdominal distention. In 48 (80%) of them, a diagnosis of migraine without aura was made. In the subgroup of 64 patients without severe postprandial abdominal distention, only 6 (9%) patients had migraine ($p < 0.001$, Chi square test). The prevalence of migraine was not different among the three subgroup of IBS.

Conclusions: In IBS patients and severe postprandial abdominal distention, a very high prevalence of migraine without aura is present. Further studies are needed to clarify whether a pathologic, diffuse activation of the nitrergic pathway is responsible for these alterations.

PO544

Psychological and behavioral factors and management

Occupational therapy's role in headache management: a lifestyle behavioral approach

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Picture 1. Topics addressed in occupational therapy headache treatment.

Outcome measures used
Canadian Occupational Performance Measure (COPM)
RAND SF-36
Headache Impact Test (HIT-6)
Headache Management Self-Efficacy Scale (HMSE)
Migraine Disability Assessment Scale (MIDAS)
Migraine Specific Quality of Life Questionnaire (MSQL)

Picture 2. Outcome measures used

Preliminary demographic outcomes	
Total participants	200 participants
	Female: 77%
	Male: 23%
Primary diagnoses	Migraines: 66%
	Headache: 17%
	Occipital Neuralgia: 4%
	Other head/face pain diagnoses: 12%
Average age	39 years old
Average number of sessions received	4.78

Picture 3. Preliminary demographic outcomes

Background: Occupational therapists (OTs) offer a vital perspective on behavioral, emotional, and other non-pharmacological headache treatment approaches to improve patient self-management of headaches, yet OTs' involvement in comprehensive headache care is relatively infrequent. The aim of this study is to explain the role of OT in headache treatment, and present the outcomes of a program development study.

Methods: This was a retrospective program development and quality improvement study that collected and assessed clinical outcome data of patients who entered an outpatient OT program for headaches. An OT lifestyle modification approach was used, which has been shown to develop health-promoting habits and routines for improved health management and disease prevention. Examples of topics addressed are shown in Picture 1.

zatients were referred to OT by primary care physicians, neurologists and pain specialists. Patients were pursuing usual courses of treatment, and there were no clinical interventions administered that differed from regular care. Participants completed outcome measures at admission, 8th session, and at discharge. Outcome measures used are described in Picture 2.

Results: The clinical outcomes of this quality improvement study are currently being entered and analyzed and will be available for the conference. Preliminary demographics are shown in Picture 3.

Conclusion: OTs can provide vital treatment for patients with headache disorders, helping them to improve self-management of headaches by using lifestyle modifications. More neurology, primary care, pain specialists, and headache care teams should consider occupational therapy as a part of the regular plan of care for patients with headaches.

PO545

Psychological and behavioral factors and management

Alexythimia features in chronic migraine with medication overuse

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Background: Alexythimia refers to a personality construct characterized by the inability to identify and express emotions. Previous studies agree on the presence of pathological scores of alexythimia in every headache

subtypes. It is unclear whether there is a role for alexythimia in the evolution from episodic Migraine (MIG) into Medication Overuse Headache (MOH).

Aim: To evaluate whether MOH individuals differ from MIG (with a history of minimum 10 years) as regards alexythimia scores and to investigate the association of alexythimia with illness characteristics.

Method: 89 patients suffering from MOH (N = 54; 77.8% female, Age: 41.7 ± 10.8) evolved from migraine (chronic migraine + MOH) or MIG (N = 35; 80% female; Age: 40.3 ± 8.5) were evaluated using the Toronto Alexythimia Scale (TAS-20). Diagnosis in the 2 groups was operationally defined according to ICHD-IIIβ. Data were analyzed with analysis of variance and correlations.

Results: No statistically significant demographic differences were observed between the two groups. Compared with MIG patients (42.5 ± 11.7), the MOH individuals (49.3 ± 10.0) had significantly higher scores in the TAS-20 ($p = .005$). In particular, the MOH group reported more difficulties in identifying feelings and distinguishing them from bodily sensations of emotion and in expressing feelings. Significant correlations resulted between alexythimia and illness characteristics (e.g., sensitive disturbances, perceived disability, QoL).

Conclusions: Our results indicate that MOH patients have considerably higher levels of alexythimia than MIG patients. This evidence suggests that this personality construct could be involved in the transformation of migraine from the episodic into the chronic subtype with medication overuse.

PO546

Psychological and behavioral factors and management

Psychological factors of headache

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Background: Psychological factors, such as anxiety, depression, stress and personality traits may contribute to the 60–90% of headaches acting as precipitating and perpetuating factors.

Aim: The aim of our research is to reveal some psychological correlates of headache, with special attention to personality traits and cyclothymic temperament as well as anxiety and depression. Two headache categories have been selected; individuals suffering from migraine and tension-type headache.

Method: The Beck Depression Inventory, BDI, the Headache Questionnaire, and the shortened version of NEO-PI-R and TEMPS-A were used, and also a visual analog scale for monitoring the intensity of headache.

Results: Using regression analysis, the variance of headache intensity was best explained by depression, anxious and hyperthymic temperament. Regarding headache frequency, depression, anxious temperament and neuroticism explained the biggest part of the variance. Concerning duration of headache, the variance was explained mainly by depression, anxious and cyclothymic temperament. Individuals with tension-type headache scored significantly higher at the scales of anxiety, anger and hostility, vulnerability and persistence. Those with migraine-type headache showed significant differences at depression, assertivity and positive emotion scales.

Conclusions: Psyhological factors significantly correlate to the intensity, frequency and duration of headache. Our research confirmed the literature concerning the subtypes of headache, except certain personality traits, revealing new outcomes in this field of study.

PO547

Psychological and behavioral factors and management

Migraine and theory of mind

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Background: Pathophysiological studies in migraine between attacks have shown a lack of habituation for evoked potentials. Higher order information processing is involved, when, in social situations, facial expressions are interpreted to correctly attribute mental states to persons (theory of mind, TOM).

Aim: to investigate whether in migraine without aura patients (MO), TOM differs from healthy volunteers (HV).

Method: 30 MO, paired with 30 HV matched for age, gender and profession were recruited from the general population. Susceptibility to migraine was measured with the 'Queen Square Migraine score'' (QSMS). The 'Reading the Mind in the Eyes test'' (RME) was used to measure the ability of TOM. Depression and anxiety were controlled using 'Beck Depression Inventory'' and 'Beck Anxiety Inventory''. Statistical analysis consisted of the Spearman and Mann-Whitney-U tests and linear regression.

Results: Migraine patients did not differ in the RME from HV. In MO the RME score correlated with the QSMS ($p = 0.02$). MO did not score higher than HV in the Beck Depression Inventory or the Beck Anxiety Inventory, but the anxiety score correlated significantly with the QSMS ($p = 0.042$).

Conclusion: In our population of mildly affected migraine patients, the degree of 'migrainousness'' seems to determine the ability to correctly attribute mental states to other persons. Some of the abnormalities in sensory information processing in migraineurs might be linked to an advantage in social interaction. This might be regarded as a possible benefit of the common, genetically determined disorder, migraine, that might counteract the disability caused by the headache syndrome.

PO548

Education for clinicians and patients

Paranasal sinus nitric oxide and migraine: a new hypothesis on the sino rhinogenic theory

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Migraine is a debilitating illness that has no exact bio molecule to explain its pathology. Diffused paranasal sinus nitric oxide in the nasal mucosa could be the primary molecule that initiates migraine and is termed Sinus Hypoxic Nitric Oxide Theory. This hypothesis regards repetitive or intermittent activation of the trigeminal sensory nerve and blood vessels in the nasal mucosa. Production of paranasal sinus nitric oxide is mainly induced by hypoxia due to several independent factors and the diffusion of paranasal sinus nitric oxide depends on the vulnerable surface area in the nasal cavity.

Apart from the known trigeminal nociceptive impulse in the migraine, two main peripheral trigeminal nerve activating mechanisms may induce migraine. The nerve impulses of the trigeminal sensory nerve, projected at trigeminal nucleus caudalis to the central nerve system and low plasma magnesium due to the consequence of shear stress gives rise to the symptoms of migraine. Indeed this article explains a new pathophysiological initiation between sino rhinogenic nitric oxide effects and migraine and provides an initial step for the obscured or neglected etiologically important neuro vascular impulse generating pathway. A standard surgical and medical management of migraine that links with the sinus hypoxic nitric oxide theory may restore the hypoxic state or reduce or remove the paranasal sinus nitric oxide diffusing surface. It warrants clinical testing.

PO549

Education for clinicians and patients

Ni espere. A novel mnemonic in Spanish for bad headaches

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Background: There are mnemonics in English to aid in headache management. As far a we know, there are none in Spanish.

Objective: To communicate a novel mnemonic to remember the headaches to be concerned of.

Methods: We reviewed the English and Spanish headache literature to find out the symptoms or signs or the clinical data that indicate headaches that require urgent or specialist evaluation or imaging. We designed a mnemonic in Spanish that can be used by any non headache specialist and for teaching porpoises. The mnemonic is:

NI ESPERE (don't wait), that means:

Neurosignos/síntomas (neurological signs/symptoms)

Intoxicaciones o sospecha de uso de drogas/medicamentos (intoxications/use of recreational/prescription drugs)

Edad (age)

Sistémicos, signos/síntomas (systemic manifestations)

Patrón diferente (change of clinical pattern)

Esfuerzo, (effort, headache that appears or aggravates with physical effort or Valsalva's)

Repentino, (sudden) headache that is sudden, maximal from the beginning.

Embarazo (pregnancy). Headache that appears or aggravates during pregnancy.

Conclusions: We hope that this mnemonic can be an aid in the teaching or management of headaches by all the physicians in the Spanish speaking countries.

PO550

Education for clinicians and patients

Migraine with chief complaint of prominent gastrointestinal symptoms: an under-recognized subtype

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Background: Migraine-related nausea and vomiting are usually accompanied with severe and disabling headache attack. However, there is a unique subgroup with chief complaint of prominent gastrointestinal (GI) discomforts rather than of headache. We aimed to identify such migraine patients, investigate their distinctive characteristics, and report clinical outcomes.

Methods: In this case-control study, case subjects were defined as patients who had first visited the gastroenterology clinic with chief complaint of nausea and/or vomiting, but then referred to the headache clinic because of concurrent headache. Odds ratio (OR) and 95% confidence interval (CI) were calculated to assess the distinguishing characteristics for case subjects compared to control subjects who met the migraine criteria.

Results: Over the 1.6-year study period, we identified 51 eligible case subjects (mean age: 44.2 ± 14.9; 43 females), of which 80.4% and 19.6% were compatible with the strict and probable migraine criteria, respectively. Control subjects were 1:1 matched with case subjects based on age, sex, and aura. In multivariate testing, case subjects were associated with mild-to-moderate headache intensity (OR: 6.54, 95% CI: 2.22–19.24), and inversely related to drinking alcohol (OR: 0.14, 95% CI: 0.03–0.67) and aggravation by routine activity (OR: 0.20, 95% CI: 0.07–0.59). At the 2 month follow-up visit, 82.2% had a favorable outcome in migraine management.

Conclusions: Case subjects were likely to have modest headache, which could cause difficulty in its proper diagnosis and treatment. Our findings suggest that physicians should investigate for the presence of migraine in patients with prominent GI symptoms and concurrent featureless headache.

PO551

Education for clinicians and patients

Headache histories taken on the web uncover an unusually high percentage of migraine aura

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Objective: To determine whether web-based histories collected on line would reflect the same frequency of migraine aura as those collected through structured interviews.

Background: In order to make an accurate diagnosis of headache, a thorough medical and headache history is essential. However, the accuracy and completeness of the history is dependent on the questions asked and the interpretation of the answers. Structured interviews, while better, are still subject to scripting bias and the examiner's interpretation of oral response. To date, a validated history that strictly adheres to ICHD 3 beta criteria that is obtained systematically, independent of administrator variability, has not been well studied.

Purpose: To address this issue we used a proprietary, validated instrument that defines aura according to ICHD 3 beta criteria to identify and characterize aura in a sample of patients seeking care for headache.

Methods: BonTriage, a rules-based headache history platform developed by authors Cowan, Blythe and Rapoport, is comprised of an interactive, web-based computer algorithm that utilizes forward-chaining diagnostic and generative production rules. Patients were directed to the website by their physicians prior to their initial office visit and asked to complete a questionnaire. Each

internet-obtained detailed history was transformed into a succinct narrative report including diagnostic impression, based on historical elements that matched ICHD 3 beta criteria. An average of more than 190 data points were collected from each participant, with a range of approximately 50 to 350 data points per questionnaire, depending on the complexity of the patient responses. The range reflects the dynamic nature of the questionnaire and varying levels of completion by the patient. Patients who did not complete the questions necessary to drive the rules engine were dropped, but otherwise the series was unselected. The platform is housed on a dedicated website and the data are stored on a HIPAA-compliant server. All patient data are de-identified.

Results: Accuracy for migraine vs non-migraine diagnosis was previously measured at 97%, using board certified headache specialists as the gold standard. Of the 1045 questionnaires reviewed, 39.6% (414) of the patients answered that they had experienced aura, while 60.4% (631) answered they had not. In this evaluation of the data, the percentage of patients that experienced aura is relatively high, but not outside the range that would be expected in the headache population. 22% of patients described blind spots in their vision or seeing visual distortions off to one side, while only 8% described seeing geometric patterns. When asked what percentage of their headache attacks were associated with visual aura, most patients answered either $\leq$9% or 90%.

Conclusions: This preliminary evaluation demonstrates that a web-based instrument can serve to identify aura among patients with migraine and the prevalence is consistent with numbers reported in the literature. Therefore the system can act as an aide to the physician in the efficient and accurate diagnosis of headache. The process is highly dependent on the rules engine and the accuracy of patient data entry. While this study significantly removes the tester as a variable, it does introduce additional questions regarding patient self-selection, comprehension of the questions and other issues associated with self-directed instruments. It demonstrates the potential for utilizing web-based histories. It is likely that computer-based platforms will increasingly be used as a tool to aid in the optimal diagnosis and management of headache, as well as a comprehensive resource for clinicians and researchers in the field of Headache Medicine.

PO552

Education for clinicians and patients

Barriers to recovery from concussion

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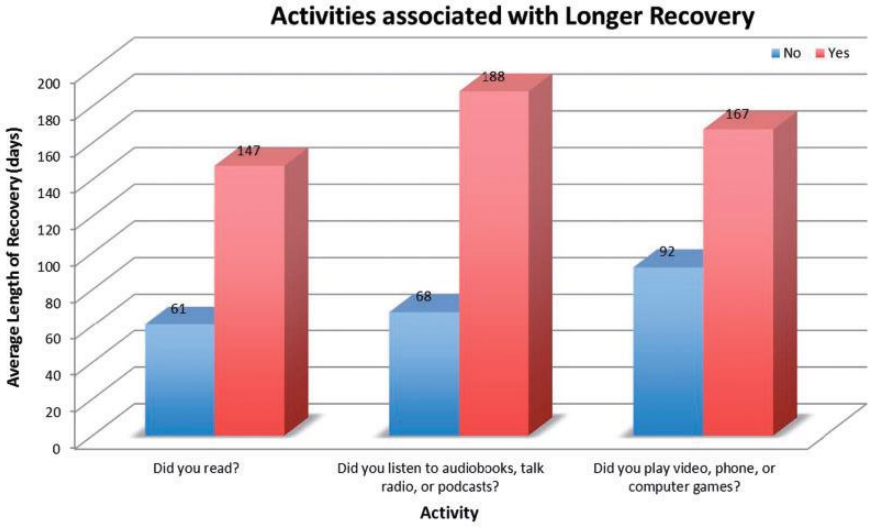
The prescribed treatment for concussion is physical and cognitive rest. Physicians and patients struggle with defining the prescription of 'rest' and also understanding the consequences of compliance.

This study attempts to determine factors which influence recovery from a concussion and to investigate the correlation between duration and quality of prescribed rest and recovery time.

Patients between the ages 10 and 50 years seen for a concussion were asked to complete a questionnaire regarding their activity during their recovery period. A total of 220 patients were asked to participate from November 2011 - May 2014 and 45 had completed it by this time.

On average, females had a longer recovery time compared to males (116 versus 97 days, respectively). Alcohol ($p = 0.126$), cigarette ($p = 0.037$), and marijuana ($p = 0.003$) consumers/users had a far greater recovery time. While many activities were associated with longer recovery times, only reading ($p = 0.028$) and listening to audio books/talk radio/podcasts ($p < 0.001$) were statistically significant. Patients who played video/phone/computer games had nearly double the recovery time compared to those who did not play those games. Patients who had previous concussions had a recovery length 3.5 times longer than first time concussion patients ($p = 0.011$).

Gender, pastimes, alcohol and substance consumption during recovery, and prior concussion history have a significant impact on recovery time. Females have a more difficult time recovering than males and suffer symptoms for greater lengths of time. Simple activities, such as reading or audiobooks, may in fact impede recovery. A history of multiple concussions poses greater challenges during recovery.



PO553

Education for clinicians and patients

Migraine and hypothyroidism: a possible comorbidity?

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Background The International Classification of HeadacheDisorders (ICHD-3 beta) includes in the secondary forms the headache attributedto hypothyroidism (HT). This condition seems to be rare in clinical practice,whereas it is more common to see migraine patients also affected by HT.

Aim This study is focused on therelationship between headaches and HT.

Method We retrospectively evaluated the clinical records of 3,962 patientsreferred to our Headache Centre from 2009 to 2013. We studied the prevalence ofHT in primary headache sufferers.

Results The population consisted of 2,294 patients with migraine without aura (MO), 861with tension-type headache (TTH), 259 with migraine with aura (MA), 190 with MO+ MA, 162 with chronic migraine (CM), 127 with cluster headache, and 69 withother primary headaches. Overall, 110 cases (106 females and 4 males) offullblown HT requiring hormone therapy were observed. Of these cases, 102 (3males) were migraineurs and 8 suffered from TTH (1 male). Therefore, the prevalenceof HT was 3.5% in migraine and 0.9% in TTH.

Conclusion HT was found in a notable proportion of migraineurs, andinterestingly HT occurred after migraine onset in 97 patients (95.1%). No caseof headache attributed to hypothyroidism (HT), according to ICHD-3 beta, wasobserved. In meta-analyses of population-based studies the prevalence of HT inthe general population resulted to be 3.05%. In our clinic-based survey theprevalence of HT in migraineurs was 3.5%. HT should be considered as a furtherpossible migraine comorbidity, even if pathophysiological mechanisms remainunclear.

PO554

Education for clinicians and patients

Headache and EEG, hype, hope and hazard

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Objective: Headache disorders are clinical syndromes defined by historical criteria. TheEEG is not included in the diagnostic criteria of the International HeadacheSociety for migraine or other major headache categories.

Objective: Studies designed to determine whether headache patients have an increasedprevalence of EEG abnormalities report conflicting results. By this study weare trying to spot light and solve this dilemma, knowing that the onlywell-matched controlled studies to address this

question found that there wasno increased prevalence of EEG abnormalities in patients with headache.

Objective: this is a retrospective observational study upon our database of routine EEGrecorded between Sept.2014 till Dec.2014. 290 EEG records have been screenedand from which 29 record with a primary complain of headache only wereanalyzed.

Objective: Headache as a primary complain represents 13% from the total causes for whichthe EEG to be ordered. The reported numbers of definitely abnormal EEG rhythmsin patient suffering from headache have been consistently low (3.4%) in routineEEG.

Objective: Similar to other studies; EEG didn't improve the diagnostic accuracy for theheadache sufferer in our study.

PO555

Education for clinicians and patients

Communication patterns in physician and chronic migraine patient dialogues during routine office visits

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Background: Effective medical communication is vital to accurate diagnosis, optimizing treatment plans, and facilitating patient adherence. Recording actual physician-patient encounters is an ecologically valid and powerful approach for studying communication, not previously applied to chronic migraine (CM).

Aim: Assess physician-patient communication about CM during routine neurology office visits.

Methods: 20 neurologists recorded routinely scheduled headache visits and submitted 67 encounters with patients the physician felt had CM. Dialogues were anonymized, transcribed, and coded in the following areas: **communication methods** (visit duration, use of "ask-tell-ask" strategy, and use of open ended questions), **headache history** content areas (headache and migraine frequency, headache-related disability) as well as **communication from the doctor to the patient** (diagnosis and treatment).

Results: 35 of 67 encounters were eligible for analysis based on robust headache discussions (ie, multiple physician-patient exchanges during the dialogue). Eligible patients had a mean age of 46 and most were female (91%) and Caucasian (89%). On average, encounters lasted 11 minutes and included 17 headache-related questions; 82% were closed-ended. Headache/migraine frequency was assessed in 27/35 (77%) dialogues; only 1 used "ask-tell-ask". Headache-related disability was discussed in 8/35 (23%) dialogues; only 1 using open-ended questions. CM diagnosis was discussed in 3/35 (9%) of encounters and treatment plans were discussed in 13/35 (37%) dialogues.

Conclusions: The majority of CM physician-patient encounters were missing elements judged to be crucial to effective CM diagnosis and treatment. Improving communication between neurologists and patients may facilitate more effective CM diagnosis and treatment.

PO556

Education for clinicians and patients

The highest prevalence of CDH in Russia: why?

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Background: Factors contributing to the highest than elsewhere prevalence of CDH (10.5%, 2012) in Russia were not yet studied.

The aim of the study carried out by H specialists in cities of St. Petersburg and Samara was to critically evaluate the approaches to CDH diagnosis and treatment in Russia: 300 neurologists were interrogated by means of special questionnaire focused on customary approaches to H diagnosis, paraclinical investigations and treatment.

Results: 97.5% of neurologists used to refer patients to paraclinical investigations (MRI, Doppler, EEG, etc.) and interpreted the revealed non-specific abnormalities as an evidence of "organic lesion of brain/brain vessels"; 70.3%

considered CDH not as primary (CM, CTTH) but related to secondary conditions; diagnoses of CM and MOH were lacking (Table 1). The majority of neurologists recommended for H prophylaxis vascular, diuretic and metabolic agents.

Conclusion: The following factors contribute to high prevalence of CDH in Russia: 1. Lack of knowledge of ICHD 2. Excessive referral to paraclinical investigations and erroneous interpretation of the results as an evidence of organic brain/vascular lesions. 3. Assigning wrong diagnoses masking true primary H diagnoses. 4. Wrong treatment strategies, leading to ineffective treatment, medication overuse and H chonification. Education in H field must be markedly intensified.

PO557

Education for clinicians and patients

Delphi survey for the development of a consensus-based test battery for headache assessment

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Background: Scientific evidence about physical signs and symptoms in the neck of different headaches is scarce beyond those used for some classification purposes. Several physical assessments are proposed but their clinical usefulness for different headache types remains to be evaluated.

Aim: To develop a consensus-based cervical test battery for the assessment of headache to identify distinct features of different headache populations.

Methods: Twenty international experts in headache were invited to participate in a Delphi survey. The first round asked participants to rate (5point Likert-scale) the usefulness of published assessments identified in a systematic review and to suggest additional tests. In the second round, these additional tests were rated for their usefulness. Results of both rounds were analyzed by identifying the median value of usefulness for each test. Tests considered "not useful" were omitted from the battery.

Results: Fourteen (n = 14, 70%) participants completed both rounds. From the initial 15 suggested tests, 4 were omitted and 3 further tests were regarded as useful for specific clinical situations. Eight additional tests were suggested. The final test battery included: head position, active range of motion, flexion-rotation test and other combined movements, trigger points, muscle test of the shoulder girdle, cranio-cervical flexion test, joint palpation, thoracic spine screening, reproduction and resolution (sustained technique), and passive physiological inter-vertebral movements.

Conclusion: An international consensus including 10 cervical physical assessments as a minimum standard for the use in headache was proposed. Recommendations for future research include further tests of validity and pilot testing.

PO559

Education for clinicians and patients

Knowledge regarding migraine and preferences for resources in a cohort of 200 migraineurs

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Background: Self-management is an important aspect of migraine care. The baseline level of knowledge of patients influences the educational strategy. Patient's preferences have to be considered when selecting resources for a headache center.

Aim: To describe the previous learning about migraine and determine patients' preferences regarding resources at the center.

Methods: We prospectively studied a cohort of new patients referred for migraine with a questionnaire.

Results: 200 migraineurs were recruited and 88.0% were women. Mean age was 40 years old with a standard deviation of 13. Patients were episodic (22.3%), frequent episodic (45.2%) or chronic (32.5%). Amongst them, 24.1% had migraine with aura and 26.0% filled the criteria for medication overuse. Their educational level was high school (13.5%), college (19.8%), or university (66.7%). 22.1% had been evaluated in a migraine clinic before the referral. Between 72.8% and 92.9% had received explanations on

different aspects of migraine management. 68.3% had previously searched the web and 34.3% had read a book on migraine. Among different resources, patients prioritized the access to a nurse (77.5% total, 57.5% first choice). Other options included educative sessions (26.1%), nutritionist (21.0%), physiotherapist (17.0%), website (16.5%), psychologist (8.5%), printed documents (6.5%).

Conclusion: Patients referred to a tertiary headache center have a high education level and many already have received or read information about migraine. A nurse should be a priority in headache center. Educational material and interventions should also be made available to a broader group of patients, and not only those followed at the center.

PO560

Education for clinicians and patients

Epidural blood patch for treatment of orthostatic headache

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Background: Epidural blood patch has been performedfor treatment of orthostatic headache related to iatrogenic and spontaneousintracranial hypotension.

Aim: This retrospective study was conductedto investigate epidural blood patch.

Methods: Data such as gender, weight andheight, cause of orthostatic headache, test for evaluating the leakage site ofCSF, injection level, the number of conducted procedures, and the baseline andpost-treatment pain intensities were collected by reviewing patients' medicalrecords. We classified the patients into two groups according to cause oforthostatic headache: spontaneous and iatrogenic group.

Results: 127 patients (149 cases ofepidural blood patch) with orthostatic headache were managed by epidural bloodpatch. The most common injection site was lumbar spine (71.1%). The averagepain intensity (5.3/10) before procedure was statistically higher than that(1.5/10) after the procedure. Most patients (83.5%) presented improvement oftheir symptom by a single procedure. 27 patients were classified intospontaneous group whereas 100 patients were into iatrogenic group. Bothdemographic data and pain intensities of each group were not significantlydifferent. The most common injection site was cervicothoracic junction (41%)in spontaneous group and lumbar spine (90%) in iatrogenic group ($P < 0.001$). The average number (1.5) ofconducted epidural blood patch in spontaneous group was significantly higherthan that (1.1) in iatrogenic group ($P = 0.007$).

Conclusions: Epidural blood patch was an effective methodfor treatment of orthostatic headache. However, patients with spontaneousorthostatic headache require repeat of procedure compared to those with iatrogenicorthostatic headache.

PO562

Education for clinicians and patients

Lesson from the expert patients. Advice for the physician to improve the care of cluster headache patients

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Background and aim: In rare disorders Expert Patients (EP) may be used to educate physicians representing an authoritative source of information about patient needs and expectations. The aim of this was to collect a list of recommendations from EP for the physicians engaged in the CH management with the purpose to improve their ability in taking care of CH patients.

Method. Patients' association providing guide and support to CH sufferers in six European countries received a letter of invitation to join to the study on April 2014. Those CH groups who accepted to participate were requested to provide a list of recommendations and advices for the physicians engaged in the CH management from at least 5 EP.

Results: Eighty-three advices from 25 EP (SP, I, UK, NL, SWE) were available for a qualitative content analysis. 77% of the EP' advices could be grouped in 7 main recommendations: 1) CH diagnosis is easy if you consider few clinical clues; 2) prescribe sumatriptan and oxygen; 3) suggest patient to not conceal and to be active in a patients' support group; 4) take patient seriously and listen to him ; 5) provide good info and be able to correct the misleading ones; 6) be sensitive to the CH consequences on the patient's significant one; 7) acknowledge that CH is a valid medical disorder that can have a significant impact on the person and support him.

Conclusion: EP' recommendations should be used to propose pragmatic patient-centered changes in healthcare services dedicated to CH.

PO563

Education for clinicians and patients

A formal analysis and synthesis: a research based standardized headache patient intake form

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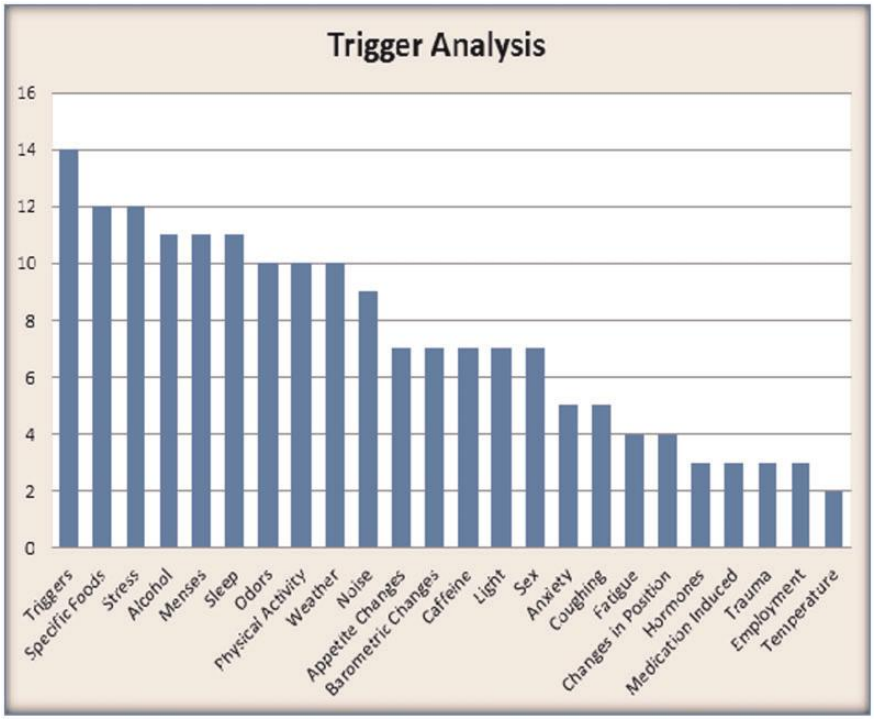
Background: The initial patient intake form is a useful tool for practitioners, establishing a first line of communication with patients. There have been no studies evaluating intake forms at tertiary headache centers. Analysis of headache intake forms at UCNS centers can provide insight into the current state today. Following analysis, establishing a research based standardized patient intake form may improve patient satisfaction/compliance, provider productivity, and data collection for future research purposes.

Objective: Analyze similarities/differences among headache intake forms from headache clinics with UCNS accredited headache medicine fellowships in the US. Establish a path towards a standardized patient intake form.

Design/Methods: Observational study where all 25 UCNS headache medicine fellowship programs were contacted and 17 forms collected. Following analysis of content/format, a panel was established, including physicians, methodologists, patients, and researchers, to gain insight using a Delphi method, to establish standardized intake form.

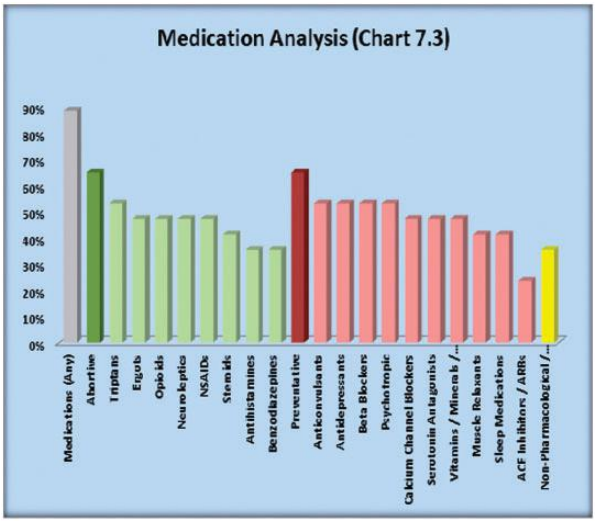
Results: Analysis of UCNS headache intake forms revealed high variability in terms of content, style, scales, and assessment tools. 8/25 headache centers have not yet established a specific headache form. Range 1–32 pages. While 80% of forms asked about family history, only 55.8% asked about PMH. After analysis, results of modified Delphi method established consensus. Standardized form will be electronic, include common data elements, in a patient friendly efficient format.

Conclusion: Analysis of UCNS intake forms demonstrated great variability. The standardized intake form



allows for efficient gathering of data for physicians treating patients and with uniform collection may prove a powerful tool in advancing headache research.

Headache Symptoms		
Parameter	**# Asked**	**% Asked**
Phonophobia	14	82.35%
Nausea / Vomiting	13	76.47%
Nasal Problems	13	76.47%
Osmophobia	13	76.47%
Photophobia	12	70.59%
Visual Disturbances	12	70.59%
Gastrointestinal Changes	11	64.71%
Energy / Mood / Personality / Mental Status Change	10	58.82%
Dizziness	9	52.94%
Scalp / Face Tenderness	6	35.29%
Weakness / Numbness	6	35.29%
Neck Stiffness	5	29.41%
Aggravated by Movement	5	29.41%
Sleep Disturbances	5	29.41%
Urinary Symptoms	5	29.41%
Jaw Pain	3	17.65%
Chills	1	5.88%
Fever	1	5.88%
Night Sweats	1	5.88%
Swollen Breasts	1	5.88%
Teeth grinding	1	5.88%
Relieving Factors	11	64.71%
Ability to Function	8	47.06%



PO564

Education for clinicians and patients

ICHD-3 beta: something is going to be lost

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Introduction: Osmophobia (Os), has been described as an accompanying symptom of headache, much more relevant in migraine (M) among primary headaches (PH) and very specific in the differential diagnosis between M and tension-type headache (TTH). In 2004 Os was included in the ICHD-2 appendix (A1.1) among the proposed diagnostic criteria of M but in 2013 in the provisional version of ICHD-3, it disappeared, without explanations.

Aim and method To understand this choice, we reviewed the literature on the subject. A search on MedLine of the term '*osmophobia*" yielded 97 articles published after the release of ICHD-2. Of these, 33 were eligible: 23 investigated Os as an accompanying symptom and 10 focused on Os as a diagnostic criteria. We calculated the cumulative values of sensibility and specificity of OS in the differential diagnosis of M within PH.

Results and conclusion The articles confirm a much higher prevalence of Os in M (up to 86%) within PH, particularly vs TTH. Even if sensibility and specificity range from 26 to 86% and 69 to 100% respectively in different papers, all authors support the usefulness of Os in the differential diagnosis between M and TTH. Calculated cumulative values demonstrate a high specificity, between 86,48% and 98,34%, of Os in in the diagnosis of M. On this ground, the unexplained decision to remove Os from the diagnostic criteria of M in ICHD-3 appears unjustified and we suggest a revision of this choice is therefore appropriate.

PO565

Education for clinicians and patients

Primary headaches and work: health oversight and criteria for judgement of suitability

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Primary headaches accounts for 90% of all the forms of headache. This disease occurres highly in the working-age population, with significant social impact. These aspects carry important economic costs calculated as loss of working days and labour productivity. In occupational setting, several circumstances are known to trigger cephalalgic attacks, for example the interruption of the circadian sleep-wake rhythm, physical/mental distress, not ergonomic postures, prolonged use of display screen, acoustic discomfort.

The aims of this study are: to provide useful information to occupational physicians on the management of workers suffering from primary headaches, to the formulation of the judgement of suitability and to the planning of the work; to identify the preventive measures to reduce the probability of recurrence of headache attacks and to ensure workers efficiency.

We identify three critical factors: the form of primary headache, the characteristics of the work and the effects due to pharmacological therapy. On the basis of these considerations we suggest guidelines for a flow chart aimed to understand worker's suitability and to guarantee safety and health.

A decision process for judgement formulation articulated in different steps (history, neurological examination and the periodic verification of the adherence to treatment prescribed) can guide the physician to identify the characteristics of the headache and the appropriate measures to take.

Primary headaches are "social" diseases; the phyisicians have to consider their impact on work, and can formulate a true judgement of suitability only after a right evaluation of their characteristics, that can be made with simple but basic steps.

PO566

Education for clinicians and patients

M-health in migraine: results in first 90 patient monitored with "mymigraines" community

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Background: Mobility technologies, along with its ecosystem of apps, have created a new model for health care. Electronic diaries are useful tools in the therapeutic strategy in migraine patients, but they could also be used to establish a follow-up care via telemedicine.

Aim: Describe our experience in first 90 migraineurs monitored with "MyMigraines" community

Methods: We designed "MyMigraines" app as a diary that allows migraineurs to collect, using their own mobile devices, characteristics, accompanying symptoms and precipitating factors of headache episodes, as well as symptomatic drugs used and impact on daily living, including visits to an emergency room. "MyMigrainesPRO" is an app complementary to "Mymigraines" that allows doctors to check, using also their own mobile devices, the evolution of each of their patients. All this information is displayed in calendars. Messages may be sent through both devices.

Results: During three months (November 2014 – January 2015) we have invited 90 migraine patients attending our Headache Unit to join "Mymigraines" community. For each patient we activated an alert system. We were noticed if patient presented more than 10 migraine days or more than 10 days of triptan intake during previous month, and if an emergency room visit was needed. Thirty one alerts were so activated during inclusion period. In 14 of them (45.1%) an additional in-office visit was established and in the rest we sent messages to our patients in order to suggest specific behaviors.

Conclusion: With "Mymigraines" community we improved the communication with our migraine patients towards a personalized therapy.

PO567

Education for clinicians and patients

Neolatin group on headache – the spoken languages of men and the international transmission of scientific knowledge

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Background - This initiative stems from previous projects[1] designed to benefit a category of people who live a particular linguistic "disadvantage": the immigrants. Even more so, those immigrants who suffer from Chronic Headache and its comorbidities (physical/psychological disorders).

Aim: To develop and share a more readily comprehensible and accessible model of communication relating to head pain and emotional-affective comorbidities. The model takes into account suggestions, needs and preferences by the main stakeholders (scientists, general doctors, patients).

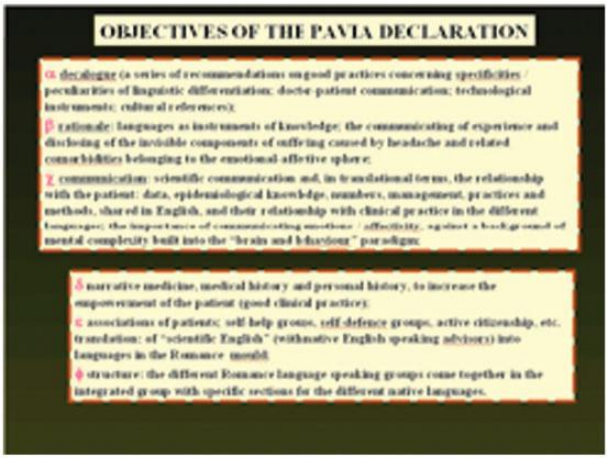
Method: The conceptual core of the Project is the Pavia Declaration (2013), which emphasizes the importance of the interplay between linguistics and neurology. It comes 1200 years after the "official" birth of the Romance languages: the Council of Tours, organised by Charlemagne, when it was explicitly stated that bishops should «*translate (transferre) their sermons in a comprehensible way, into the rustic Roman or German tongue (in rusticam romanam linguam aut thiotiscam)*» so that everyone would be able to understand.

Within the initiatives of the Pavia Declaration, we created and implemented a website (www.neolatingrouponheadache.net) containing several sections.

Results: During 2014, we recorded more than 1500 contacts from Euromediterranean, LatinAmerican and Euroasian areas. These generated several lines of suggestions about contents and research topics.

Conclusions: We believe that this way of sharing information and culture, under a scientific and structured control, is a useful means to share knowledge and valorize patient empowerment.

[1] Among others "Genetic-Ambiente Colombo 2000" Project (1995–2005) with Italian/Argentinian Health Ministries, Mondino Foundation/CBIM/University (Pavia), Latinamerican Hospitals and Universities (Argentina and Uruguay).



PO568

Education for clinicians and patients

Multidisciplinary integration of providers in an academic headache center

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Objectives: Improve access, diagnosis, and treatment of headache in a resource-challenged health care system.

Background: Chronic headache is a public health problem. New solutions are needed to provide care to the millions who need it. University of Utah is a UCNS academic certified headache center serving a 7 state catchment area (average referrals of 400/month) with 1.5 full time equivalent (FTE) headache providers. Ten University community clinics sharing an electronic medical record (EMR) contribute 25% of the headache referrals (~100 referrals month), providing an opportunity to test new approaches.

Methods: Embedded referral queue within shared EMR – diagnostic and decision support integrated into referral pathway.

Primary care provider in headache clinic at 0.05 FTE.

Anesthesiologist trained in pain medicine in headache clinic at 0.2 FTE

IRB approved for continuous data gathering, quality improvement

Results/expectations:

-provider who comes from the 'culture' of the referring pool will better understand needs, serve as more effective ambassador between primary and subspecialty care

-leveraging resources of primary care system will allow system-wide changes – e.g. patient and provider education on migraine diagnosis, discouragement of opiate use, etc.

-integration of primary care approaches to subspecialty care, and vice versa, will generate unforeseen ideas, efficiencies, solutions

-provider trained in pain medicine brings new ideas to headache management

-integration of primary and subspecialty teams anticipates the reality of accountable care – care delivery as well as revenue models

Conclusions/future directions: If successful our model is scalable, allowing the dissemination of subspecialty headache care to the entire delivery system.

PO570

Headache in history and the arts

Picasso and de chirico were not migraineurs

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Background Some authors suggestedthat migraine aura may have represented an inspiration for unusual andrecurrent features of paintings by Pablo Picasso and Giorgio De Chirico. Amigraine hypothesis was formulated for Picasso's art, based on aura-like patterns,such as illusory vertical splitting and shifts of the eyes. As for De Chirico,the jagged effect of water, the spiky silhouette of a knight, a black sun motifintruding into an interior scene were interpreted to be evoked by aura.

Aim **We looked for further evidence toexamine in depth this hypothesis.** MethodWe read Picasso's biographies and De Chirico's autobiography, evaluatingtheir pictorial works.

Results InPicasso's biographies there is no report of the artist suffering throughout hislong life from any particular illness, migraine included. The style characterizingthe portraits of female models that could resemble migraine aura seems to be anevolution from the previous Cubist period. De Chirico started painting theblack sun motifs when he was over 80, an age when the occurrence of aura isextremely unusual. Conversely, other neurologists objected that the availableevidence inferred from artist's autobiography suggests a diagnosis of temporallobe epilepsy rather than migraine.

Conclusion To prevent an inflated use of the said diagnostic attribution in pathographicstudies of celebrated artists, a methodological standard should be fulfilled instudies of migraine aura as artistic inspiration. The diagnosis of migraineshould be supported by semi-/autobiographical writings and/or contemporaries'observations in addition to the evidence derived from the analysis of theartworks.

PO571

Headache in history and the arts

Medical school of salerno and headache: clinical and therapeutic aspects

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Maestro Salerno, teacher of Medical School of Salerno, distinguished "cephalea" in wich pain is total from "migraine" which affects " a single side of the head" ("Magister Salernus,Catholica cod. 1506). Pathogenesis was explained according to the humoral theory involving external and internal factors; stress, alcohol, indigestion, excessive use of drugs, unbalance of organical humours. Pain distinction was very accurate: keen, periodical, irregular, persistent, continous and serious pain. Cephalea way be caused by blood and its typical symptoms are a sensation of burning and heavy forehead, beating of arteries, dilation of veins. Diagnosis was also supported by a detailed urinary semeiology: urin could be flowing and fatty if cephalea was provoked by bile.

Maestro Bartolomeo described migraine as "a pain in the middle part of the head or on the right or the left side, provoked both by blood and by other humours". Attacks of migraine can be very frequent and may take place at intervals of days or even weeks.

Treatment was prescribed according to the probable causes of pain, which are:

- sleeping in the afternoon;
- alcohol were considered as a primary cause of severe cephalea;
- milk was considered harmful.

One of the remedies was coffee, which still today is largely used, as caffeine, in anti-migraine drugs. Other simple remedies, such as roses, antimony (used for chronicle cephaleas) were also recommended.

In conclusion, Medical School of Salerno individuated the difference between a diffused (tensive) cephalea and migraine, suggesting remedies and diets, some of which are still effective.

PO572

Headache in history and the arts

The history of caffeine in the treatment of headache

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Background: Historically, many herbal headache remedies were comprised of caffeine containing substances. By the late nineteenth century, pharmaceutical companies used refined caffeine in combination with early anti-inflammatories in a range of remedies. These treatments persist to the current day.

Aim: To review the history of the derivation of refined caffeine, illustrate the range of treatments that have contained it over the last 150 years and describe the role that it has played in headache treatment.

Method: A literature review of articles, books and primary source material from the nineteenth, twentieth and twenty first century which detail the use of caffeine in headache treatment combined with images obtained from a collection of Victorian era headache treatments. The evolution of the use of caffeine was organized and set into historical context of the industrial revolution.

Results: Coffee was first used in the mid 15th century. Its role for treating ailments was described over several centuries. The nineteenth century saw caffeine used in combination with painkillers and anti-inflammatories for headache. The twentieth century saw it combined with ergotamines and used intravenously by 1944 for post dural puncture headaches. It remains one of the most commonly used remedies for headaches, both as a food and as a medication.

Conclusion: Caffeine remains an important tool in the common treatment of many headache subtypes. We have reviewed the history of caffeine, its refinement and its use in a range of medications for the treatment of headache.

PO573

Headache in history and the arts

Headache and arts

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Background: Portrayal of the headache is a universal phenomenon overarching the human history of culture. It is a revolving moment in the different aspects of fine arts from the archaic ages to the contemporary arts. The human artist represents the own phenomenon with the involved suffering and demonstrates the wide repository of cure trials.

Aim: We look for the identity in the presentation of headaches without reference to historic age and cultural background. We analyze the various illustrations and highlight the emotional and aesthetic differences between typical portrayals.

Method: We survey the portrayals of headaches, connected states, symptoms and treatment methods with the analysis of

1. Cave paintings

2. Drawings of Egyptian papyri

3. Ancient Hellenic-Latin artworks

4. Artworks of Christian fine arts

5. and the contemporary arts.

Result: The focus of these artworks is the suffering human being in every case. Both deep empathy and unbiased eexemplification are discoverable in the representations. The proximity and the style of communication with environment is varying from isolation to total participation. Fundamental identity is established in the portrayal of headaches from the viewpoint of similar posture, pathos and the mechanic and practical way of pain alleviation.

PO574

Headache in history and the arts

The artemicranica project

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Background: The project "ARTeMICRANICA" originates from the exhibition of Giorgio De Chirico 'ARTeMICRANIA. Opere e parole tra mal di testa e metafisica." held in Rome in September 2003 at the XI Congress of the International Headache Society / IHC 2003.

Aim: The goal is to enhance the artistic manifestation of a pain "invisible" as it is the migraine, through the creation of a virtual gallery of works of art (paintings, drawings, etc), made by headache and not of all ages. Externalize and share artistically migraine pain can be of great help in this persons helping to not cut themselves off. This is the aim of "ARTeMICRANICA".

Method: The project makes use for communication of a website: www.artemicranica.org, containing the different 'artistic" projects, with the aim to involve and activate people with migraine (or that have had experiences of "headache") to describe and represent, graphically and verbal, such experiences.

They will also be treated issues related to the quality of life of patients and migraine aura, a heritage of "experiences" that in some cases can be a "gift."

Results: The works, considered artistically always expressive, are sketches of graphics with or without the integration of words, all still made instinctively, resulting from a strong personal reaction, even those which appear to be very expressive. In addition, special attention is given to the children of the middle school, as happened in the past.

Conclusion: An example of web technology at the service of patients, for the dissemination and sharing of experiences.