Scientific Session I

ScS1-1

The prevalence of primary headache disorders in Russia: a countrywide population-based survey

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Objective: To estimate the 1-year prevalences of episodic headache disorders (migraine and tension-type headache) and of headache occurring on ≥15 days/month, and identify their principal risk factors in the general population of Russia.

Methods: A countrywide population-based random sample of 2,725 biologically unrelated adults in 35 cities and nine rural areas of Russia were interviewed in a door-to-door survey using a previously-validated diagnostic questionnaire.

Results: Of the 2,725 eligible adults contacted, 2,025 responded (females 52.6%, mean age 39.5±13.4 years). Of these, 1,273 (62.9%) reported headache “not related to flu, hangover, cold, or head injury” occurring at least once in the previous year. The overall 1-year prevalence of migraine (All-MIG) was 20.3% (95%CI18.5-22.1), of which definite migraine was 9.5% (95%CI8.2-10.8) and probable migraine 10.8% (95%CI9.5-12.2). Risk factors for All-MIG were female gender (OR 3.8; 95%CI2.8-5.1) and obesity (OR 1.5; 95%CI1.1-2.1). The 1-year prevalence of All-TTH was 30.9% (95%CI28.9-32.9), of which definite TTH was 25.4% (95%CI23.5-27.3) and probable TTH 5.5% (95%CI4.5-6.5). All-TTH was more prevalent in urban than in rural areas (OR 1.6; 95%CI1.3-2.0).

Headache on ≥15 days/month was reported by 213 (10.5%) respondents. Low socioeconomic status (OR 3.4; 95%CI2.4-4.9), obesity (OR 3.0; 95%CI2.1-4.3), female gender (OR 2.9; 95%CI2.1-4.1) and age over 40 years (OR 2.6; 95%CI1.9-3.6) were risk factors. The majority of these respondents (68.1%) overused acute headache medications.

Conclusion: The study demonstrated a high prevalence of migraine and a very high prevalence of headache on ≥15 days/month, and revealed unmet health-care needs of people with headache in Russia.

ScS1-2

Diagnosis of medication overuse headache (MOH): validation of a brief screening tool in Bordeaux headache centre, France

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Application of the diagnostic revised criteria for medication overuse headache of the ICHD-II classification requires clinical experience for the physician and is often time-consuming. We validated a rapid questionnaire evaluating drug-attack consumption as a screening tool.

ICHD-II criteria were transformed in questions formulated in such a way that they could be self administered, easily understood, quick filled out, and highly sensitive for MOH. We compared this questionnaire to the gold standard: the diagnosis made by headache specialists, based on the second edition of the ICHD-II.

All men and women who were visiting for MOH or migraine for the first time were consecutively included between September 2009 and February 2010. As validity
indicators, we calculated sensitivity, specificity, positive and negative predictive values of the item.

Seventy-nine patients were screened, 77 included, 2 female patients excluded. Forty-two patients have been considered as suffering from MOH, 35 patients suffered from migraine without medication overuse. The question “do you take an attack treatment more than 10 days per month” had a sensibility of 95.2 %, a specificity of 76.5 %, a positive predictive value of 83.3% and a negative predictive value of 92.9 %. This simple question can detect MOH with such a sensibility that it could be of double interest in clinical practice and research.

ScS1-3

Hyperreactivity and migraine risk: a 15 year follow-up study

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Background: Reactivity is an early temperamental trait. Hyperreactive (IPR) newborns show a low threshold of sensory stimulation and a lack of habituation to stimuli. Other symptoms of hyperactivity are frequent and persistent crying, irritability, sleep disorders, jolt at noises and other “amplificated” responses to environmental stimuli. Recent studies suggested that migraneurs have a lower thresholds of neurophysiological reactions and a lack of habituation. So, headache can be considered an amplified response too, to internal and/or external stimuli.

Aims: To evaluate, after at least 15 years, the prevalence of primary headache in IPR infants.

Methods: We got in contact with 100 children (m=60, f=40; m.a.=17.5): 50 IPR and 50 no IPR; the groups were similar for age and gender. All infants were visited between 1 to 18 months of life. We administered a revised headache’s questionnaire (2004), X² test had been used.

Results: Fifteen (30%) IPR infants suffered from Migraine (80% are 1.6.1), vs 5 (10%) of the control group (20% are 1.6.1) (p < .05); 16 (32%) suffered from TTH (62% are 2.4.1), vs 14 (28%) of the control group (71% are 2.4.1).

Conclusion: IPR is an important risk factor for developing migraine.

ScS1-4

Migraine and cardiovascular disease: the role of aspirin - subgroup analyses of the women’s health study

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Background: Migraine has been associated with increased risk of cardiovascular disease (CVD). Whether patients with migraine should be treated with aspirin to prevent CVD remains unclear.

Methods: Post-hoc subgroup analyses of the Women’s Health Study, a randomized placebo-controlled trial testing the effect of 100mg aspirin on alternate days in the primary prevention of CVD among 39,876 women.

Results: During 10 years of follow-up, 998 major CVD events were confirmed in 39,757 women with complete migraine information. Aspirin reduced the risk of stroke (RR=0.83, 95%CI=0.69-0.99), specifically ischemic stroke (RR=0.76; 95%CI=0.63-0.93) but not other CVD event. Migraine or aura status did not modify the effect of aspirin on CVD except for myocardial infarction (MI) (p-interaction=0.01). Women with migraine with aura on aspirin had an increased risk of MI (RR=3.72, 95%CI=1.39-9.95). Other subgroups did not have increased risk. Further exploratory analyses indicate that the increased MI risk is only apparent among women with migraine with aura on aspirin who ever smoked or had a history of hypertension (p-interaction < 0.01).

Conclusion: In post-hoc subgroup analyses of this large trial, aspirin had similar protective effects on ischemic stroke for women with or without migraine. By contrast, our data suggest that among migraineurs with aura, aspirin increased the risk of MI, possibly via interactions by smoking and hypertension. The small number of outcome events in subgroups, the exploratory nature of our analyses, and lack of plausible mechanisms raises the possibility of a chance finding, which must caution the interpretation. Future targeted research is warranted to evaluate this question.
ScS1-5

Comorbid depression as a predicting factor for cutaneous allodynia in a clinical population of migraine patients; report from lumina

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Objective: To investigate if comorbid depression plays a role in the prevalence of cutaneous allodynia (CA) in migraineurs.

Background: Cutaneous allodynia, the perception of pain in response to non-noxious stimuli to the skin, is a common feature accompanying migraine attacks. Allodynia represents an underlying pathophysiologic mechanism with activation of nociceptors and the development of central sensitization. Depression has been described as a potential risk factor for increased prevalence of CA but also for chronification of migraine.

Methods: We sent out a digital questionnaire on migraine and depression to 2,582 self-reported migraineurs, aged between 18 and 74, from the LUMINA-database. Allodynia was estimated by a validated 12-item questionnaire. Depression was diagnosed based on an algorithm, including validated instruments (HADS-D, CESD, additional questions on lifetime depression).

Results: Two-thirds (67.2%) of migraineurs reported CA during migraine attacks. Female migraineurs reported more often CA (OR 3.3 [95% CI 2.3-4.7]). Multivariate logistic regression, adjusted for age, sex, attack frequency, migraine type and use of prophylactic agents showed that migraineurs with CA had significantly more often a lifetime depression than migraineurs without CA (OR 2.2 [95% CI 1.3-3.6]).

Conclusion: This large study shows that two-thirds of migraineurs have CA during their attacks, with a preponderance in female migraineurs but most importantly in migraineurs with lifetime depression.

ScS1-6

Chronic daily headache is associated with somatoform vertigo and dizziness

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Objective: To determine the degree of co-morbidity between chronic daily headache (CDH) and daily forms of somatoform vertigo and dizziness as link to understand the mechanisms underlying the development of chronic disease.

Methods: 1160 patients with vertigo or dizziness were recruited prospectively from a tertiary dizziness center between March 2010 and January 2011. All patients completed a specific questionnaire assessing whether they had headache and at what frequency over the last year in addition to their dizziness or vertigo diagnosis that was assessed clinically.

Results: Patients with primary or secondary somatoform vertigo (phobic postural vertigo; N=402) suffered significantly more often (8.7%) from chronic daily headache (≥15 headache days/month) compared to true vertigo or dizziness patients (N=239; unilateral or bilateral vestibulopathy) that reported chronic daily headache in only 3.8% (p=0.017). Vestibular migraine naturally was even more associated with CDH (10.9%), while patients with menière’s disease rarely develop CDH (1.3%).

Conclusion: Our data shows a high co-morbidity rate of CDH with somatoform vertigo, which might hint at a common or generalized mechanism involved in the development of chronic disease. Central facilitation mechanisms might lead to disinhibition of afferent pathways within and beyond the trigeminal nociceptive system making patients with somatoform vertigo and dizziness more susceptible to the development of CDH. Anxiety and depression certainly play a role in both conditions and will be further investigated.

ScS1-7

Vestibular migraine - validity of clinical diagnostic criteria

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Background: Clinical recognition of vestibular migraine (VM) is still hampered by the lack of consensus Diagnostic criteria. This study evaluates the validity of clinical criteria for definite (dVM) and probable (pVM) vestibular migraine.

Methods: We re-assessed 75 patients (67 women, age 24-76y) with dVM (n=47) or pVM (n=28) according to previously published criteria after a mean follow-up of
Results: dVM was confirmed in 40 of 47 patients with a prior diagnosis of dVM (85%). Fourteen of 28 patients initially classified as pVM met criteria for dVM (50%), nine for pVM (32%). Six additional patients with dVM and two with pVM had developed mild sensorineural hearing loss formally fulfilling criteria for bilateral Menière’s disease (MD), but had clinical features atypical of MD. Seven of these also met criteria for dVM at follow-up. The initial diagnosis was completely revised in four patients.

Conclusion: Diagnostic criteria of dVM have a high positive predictive value (85%). Half of patients with pVM evolve to meet criteria for dVM. However, in a subgroup of VM patients with hearing loss, criteria for dVM and MD are not sufficiently discriminative.

ScS1-8
Associations of lipid levels with headache and migraine in the population-based epidemiology of vascular aging study
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Background and aims: Migraine with aura has been associated with increased prevalence of cardiovascular risk factors, including elevated levels of some vascular biomarkers. However, little research has been done on whether this association is observed among the elderly. We examined the associations of lipid levels with headache and migraine in a cohort of elderly individuals.

Methods: Cross-sectional study among the 1155 participants enrolled in the Epidemiology of Vascular Aging Study who provided information about headache and had available blood biomarkers. Participants were classified into tertiles for each biomarker. Headaches were classified based on headache-specialist telephone interviews, following current guidelines. We used multinomial logistic regression to evaluate the association between biomarker tertiles and headache categories, adjusting for vascular risk factors.

Results: 925 people had no severe headache, 64 people had non-migraine headache, 166 people had migraine, of whom 23 people had aura. Compared to participants without headache, we observed strong associations between increasing tertiles of total cholesterol and migraine with aura. The OR (95% CI) was 4.67 (0.99-21.97) for the 2nd tertile and 5.97 (1.29-27.61) for the 3rd tertile. We also found strong associations between triglycerides and migraine with aura (OR for 3rd tertile: 4.42 (1.32-14.77)). We did not see significant associations between increased biomarkers levels and any other headache group.

Conclusions: Results of this study indicate that elevated levels of total cholesterol and triglycerides are associated with migraine with aura but not other headache forms in the elderly. Further research is warranted to explore the role of these biomarkers in migraine with aura.

Scientific Session II
ScS2-I
Nociceptive blink reflex habituation in episodic cluster headache patients during cluster period
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Background: The precise pathogenesis of cluster headache (CH) is unknown, although several data support the central origin of CH pain. We recently observed impaired habituation mechanisms of the conventional blink reflex in episodic CH patients during the bout studying pain side only.

Objectives: Here, we have studied more selectively pain trigeminal system by recording the nociceptive specific blink reflex (nBR) area and habituation in a group of CH patients and in both affected and non-affected side.

Methods: We enrolled seventeen patients affected by episodic CH during the bout outside the attack and 18 healthy subjects (HS). We assessed pain threshold, and we recorded nociceptive blink reflex area (average of 5 rectified sweeps) and habituation (2 blocks of 5 rectified sweeps, ISI 30 sec, IBI 2 min) by stimulating the supraorbital nerve on the right side in HS and on both affected and non-affected side in ECH patients.

Results: In patients the pain threshold on the affected was lower than that of non-affected side (p=0.035) and of HS (p=0.022). The nBR reflex area was decreased in both
ECH sides (p < 0.05) with respect to that of HS, whereas nBR habituation was significantly impaired on the ECH affected side only (p=0.022 vs non-affected).

Conclusion: Our data document lateralized pathological changes of the craniofacial nociception in episodic cluster headache. In fact, decreased pain threshold and lack of nBR habituation were observed on the affected side only. This seems primarily due of changes within the higher cerebral regions of the nociceptive system.

ScS2-2

The co-morbid relationship between migraine and endometriosis: a population-based case-control study

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Background and purpose: The prior study showed endometriosis might be co-morbid with migraine. This study aims to validate this co-morbidity from a large study cohort.

Methods: Data was derived from the National Health Insurance Research Database of Taiwan, which contains outpatient and inpatient records from 1996 to 2007. Our study cohort consisted of 20220 endometriosis patients (aged between 18-51 years old) and 101100 sex- and age-matched controls without any diagnosis of endometriosis. The study period was from one year before the initial outpatient or inpatient visit for endometriosis to one year following the last visit. The incidences of migraine in the study period were analyzed.

Results: Patients with endometriosis were more likely to suffer migraine headache compared with controls in the study period for endometriosis (odds ratio [OR] 1.91; 95% confidence interval [CI] 1.62-2.26; P < 0.001). The co-morbid association between migraine and endometriosis was still significant after controlling for age, drug and surgery treatments of endometriosis, and medical histories of infertility (OR=1.66). The probability of migraine occurring before endometriosis was similar to the probability of migraine following endometriosis (ORs: 2.00 VS. 1.85). However only the association between migraine occurring before endometriosis remained after controlling confounders mentioned above (OR=2.40).

Conclusions: Our study confirms the co-morbid relationship between migraine and endometriosis, and migraine may occur before the diagnosis of endometriosis in female individuals. It merits further investigation to delineate the relationship between migraine and endometriosis.

ScS2-3

Predicting outcome after acute whiplash with a risk score system based on 2 prospective studies

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The WAD grading system (I-III) has shown limitations as a tool for predicting transition towards chronicity. From the clinical point of view it makes sense to segregate whiplash-exposed patients into different risk strata from early after injuries based on early findings. Therefore, 2 clinical prospective studies to examine the expediency of applying stratified risk assessment diagnostics to whiplash-exposed patients were concluded. Firstly a 1-yr study included 141 consecutive acute whiplash patients and 40 ankle injured age/sex matched controls. Secondly, an interventional study included 688 whiplash patients applying obtained risk factors dividing into a high (4-19pts) and a low risk (0-3 pts) group. Risk points based on an algorithm of active neck mobility, VAS neckpain/headache, number-of-non-painful complaints (0-11). It was clinically meaningful when examining data in both studies to segregate risk scores into 7 risk strata. ROC (receiver operating characteristics for non-recovery/riskscore) estimations for the studies 1: (ROC area = 0.89; 2: ROC area = 0.80). 98% in risk group 1 returned to work, in group 7 only 32% (p < 0.0001). Muscle pain by palpation (neck/jaw: p < 0.0001), by pressure algometry (p < 0.0001), all McGill PQ parameters (p < 0.0001), impact of event (p < 0.0006), initial work-assessment (p < 0.0001). MVC by neck flexion (p < 0.001); neck extension (p < 0.004) were in concordance with strata. To conclude, the risk score shows bio-psycho-socially robustness 5 days after injury. Being able to identify the patients at risk at an early point is essential for future treatment studies on treating both acute and chronic whiplash patients.
**ScS2-4**

The cost of headache disorders in Europe: the Eurolight project


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Background and aims: Headache disorders are the most common group of neurological disorders, but their monetary costs in Europe are unknown. The aim was to perform the first comprehensive investigation of how economic resources are lost in Europe because of headache.

Methods: From November 2008 to August 2009, a cross-sectional survey was conducted by somewhat different methods in eight selected countries representing 55% of the adult EU population. Participation rates varied between 11% and 59%. In total, 8,165 questionnaires were included in this analysis. Bottom-up methodology was used to estimate direct (medications, outpatient care, hospitalization, investigations) and indirect (work absenteeism and reduced productivity at work) annual per-person costs. Simultaneously-collected prevalence data were used to impute costs on national levels.

Findings: The mean per-person annual costs were €1,177 for migraine (95% CI 1,112-1,342; indirect costs 93%), €300 for tension-type headache (TTH, 95% CI 227-373; indirect costs 92%), €3,444 for medication-overuse headache (MOH, 95% CI 2,383-4,505; indirect costs 92%), and €253 for other headaches (95% CI 99-407; indirect costs 82%). In the EU, the total annual cost of headache among adults aged 18-65 years was estimated at €115 billion, apportioned to migraine (€98 billion; 63%), TTH (€20 billion; 13%), MOH (€34 billion; 22%) and other headaches (€3 billion; 2%).

Interpretation: Headache disorders have a prominent position among all health disorders as drivers of immense economic losses for the EU. This has immediate implications for health-care policy. Health care for headache can be both improved and cost-saving.

**ScS2-5**

Headache attributed to airplane travel: data from a series of 63 patients

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Introduction: Headache attributed to airplane travel (AH) indicates a new form of headache, whose attacks have peculiar features and are strictly related to airplane travel. Only few cases have been described, although AH does not seem to be so rare.

Material and methods: Following our previously published paper (Mainardi et al, 2007), we were contacted by several subjects. They were asked to fill up a questionnaire, which was evaluated directly or by phone.

Results: Up to now, 63 cases (males: 65%) were diagnosed. The pain site was mainly frontal-orbital (n=49) or frontal-parietal (n=6). A strictly unilateral side was reported in 79% of patients; side-shift in different attacks was observed in 22%. The mean age at onset was 29.5 years (range 7-62). AH attacks occurred during landing (in four, also during take off), lasted about 20 minutes (range 5-60) and remitted spontaneously. Its intensity was very severe or severe. Only in 9 cases the first attack occurred during the first flight. The attacks presented in more than 50% of flights in 15 patients; nine reported its occurrence during every flight. A possible sinus infection was ruled out. Prophylactic use of NSAIDs occasionally prevented the attacks.

Conclusions: To our knowledge, this is the largest series of AH cases. Our data confirm the attacks’ stereotyped features and suggesting this is a specific clinical entity, in
keeping with the provisional diagnostic criteria we proposed. Therefore, AH could be listed in the appendix of the ICHD-II (2), among novel entities that require further validation.

**ScS2-6**

_A basic diagnostic headache diary (bdhd) is well accepted and useful in the diagnosis of headache. A multicenter European and Latin American study_

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**Background and aim:** Through decades a number of headache diaries have been developed but there is very little information about their usability and general acceptance. We aimed to test the usability and usefulness of a basic diagnostic headache diary (BDHD) in a multicenter study.

**Methods:** Enrolled patients were randomized to 2 groups, either to

Group 1 who received the basic headache diary before the visit and were asked to fill in the diary for at least one month before their first visit or to

Group 2 who did not receive a diary prior the clinical visit.

**Results:** 626 patients completed (321/305 resp.) the study in 9 countries. The mean number of diagnoses per patient was significantly higher in Group 1 (p=0.04). Only tension-type headache (TTH) was more frequently diagnosed in Group 2 than in Group 1 (38.8% vs.25%, p=0.01). Accuracy of diary compilation was found complete in 97.5 %. The diary and the interview were complete for diagnosis in 97.7% in contrast to the clinical interview alone in 86.8% (p< 0.001). In total, 97.5% of patients and 97% of the physicians were satisfied with the diary and it was rated as very helpful for the use of medication.

**Conclusions:** The BDHD is very helpful for the diagnostic assessment of primary headaches and perceived as useful by both patients and physicians for the headache management.

**ScS2-7**

_Hypothalamic neuromodulation for refractory chronic cluster headache: experience in 5 patients treated with a modified anatomical target_

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**Background and objectives:** Hypothalamic neurostimulation has been carried out in around 20 patients with refractory chronic CH with variable results, though efficacy has been reported in two-thirds of cases. We show our experience with 5 patients who received neurostimulation with a modified hypothalamic anatomical target.

**Patients and methods:** All 5 patients (4 males, mean age 48 years) had had daily attacks of CH needing subcutaneous sumatriptan for more than 2 years (average 6 years) and had been refractory to all pharmacological treatments before the operation. There had been also refractory to aggressive treatments (including gamma-knife, thermocoagulation, suboccipital stimulation, etc). Two had severe complications of the chronic use of steroids. A tetrapolar electrode was implanted under local anesthesia and multiunit recording 4 mm lateral to the third ventricle wall, 2 mm behing the intercomissural point and 5 mm under the intercomisural line.

**Results:** After a mean time period of 54 days to optimize neurostimulation period, four patients became pain-free and have been able to retire all the medication for a period of follow-up of 1.5-5 years. The remaining patient (one year follow-up) has improved a mean of 60%. We had no relevant complications.

**Conclusion:** Our results strongly support deep hypothalamic neurostimulation as a successful treatment of desperate chronic CH patients. Our slight modification of the final target in the postero-lateral hypothalamus, trying to improve the stimulation area both by separating from the lateral ventricle wall and including the autonomic tracts going to the brainstem, could have contributed to our excellent results.

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ScS2-8

Spontaneous intracranial hypotension. A prospective series of 80 patients

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Background: Spontaneous intracranial hypotension (SIH) can be cured by epidural blood patch (EBP).

Objectives: To study the outcome in SIH treated by EBP after initial conservative measures (bed rest, hydration) without lumbar puncture to measure CSF pressure and without looking for a CSF tear.

Methods: We analysed prospective data on 80 consecutive headache patients (55 women) diagnosed with SIH between 2004 and 2009 in our institution based on severe orthostatic headaches (75) and/or typical MRI abnormalities (66), in the absence of an obvious cause of dural tear.

Results: Mean delay from headache onset to diagnosis of SIH was 24±35 days. Conservative measures cured 15 patients (mean diagnosis delay 12±14 days). EBP was performed in 64 patients (the 65th refused) and cured 77% after one (61%), two (14%) or three (2%) procedures. Patients cured by the first EBP were more likely women than men (68 vs 45%) and had a shorter diagnosis delay than those who failed (24±27 vs 29±51). A subdural hematoma was found in 19 patients (mean diagnosis delay of SIH 34±31 days) and resolved after conservative measures (0.5%), EBP (58%) or surgical drainage (26%). Compared to women, men had a longer mean diagnosis delay (27±31 vs 22±37 days) and a higher frequency of subdural hematoma (44 vs 14%).

Conclusion: Our results confirm the efficacy of EBP in SIH and show the efficacy of initial conservative measures in early diagnosed patients. Reducing the delay of diagnosis, especially in men, seems to be the “key of success” to avoid complications.

ScS2-9

Cannabinoid mechanisms of acetaminophen within the trigeminal thalamus

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Acetaminophen (paracetamol) is an analgesic frequently used by migraine and tension-type headache sufferers as a first-line treatment. However, its site of action within the CNS is not yet known. In this study we aimed to investigate acetaminophen’s potential effects within the sensory thalamus and to assess its efficacy in relation to the cannabinoid receptor 1 (CB1).

In anesthetized male rats neurons responding to electrical stimulation of dural vessels were identified within the trigeminal thalamus using electrophysiology. The actions of acetaminophen were tested on dural-evoked firing and on spontaneous neuronal activity. In a separate group, administration of a CB1 receptor antagonist (AM-251) was used as a pre-treatment to acetaminophen. Acetaminophen was further tested on dural-evoked responses within the thalamus of anesthetized CB1 knockout mice and compared to the responses of wild type littermate mice. The presence of CB1 receptors within the thalamus was confirmed by means of immunohistochemistry.

Acetaminophen significantly inhibited Aδ- and C-fiber firing in response to trigeminovascular stimulation, and reduced spontaneous firing within the rat trigeminal thalamus. Co-administration of AM-251 with acetaminophen blocked its inhibitory effects. Similarly, in wild type mice acetaminophen significantly reduced dural-evoked responses and thalamic spontaneous neuronal activity, while had no inhibitory effects in CB1 knockout mice.

The CB1 receptor is a major site of action of acetaminophen within the trigeminal thalamus. Given that acetaminophen may be implicated in medication overuse headache, understanding its pharmacology will increase our perceptive of the development of medication overuse headache and improve the treatment options for common types of headaches.

ScS2-10

Placebo analgesia in migraine: a study by laser evoked potentials

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Aims: We aimed to evaluate the effect of verbal suggestion on the pain perception and brain potentials induced by laser stimuli in migraine without aura patients compared to age and sex matched controls.

Methods: Thirty asymptomatic migraine without aura patients and twenty controls were evaluated by high density (65 channels) laser evoked potentials. Stimuli were delivered on the right hand and the right supraorbital zone after a verbal warning of no pain or strong pain, leaving unchanged the laser intensity. All patients were also submitted to anxiety and depression evaluation by the means of Zung scales, MIDAS and allodynia scores. Fifteen patients underwent preventive treatment for migraine, and were clinically evaluated after two months therapy.

Results: In control subjects, the warning of strong vs no pain caused respectively an increase vs a reduction of pain rating and P2 amplitude. In patients, there was a significant opposite effect on the P2 component, especially when the trigeminal zone was stimulated. The increase of P2 amplitude in the no pain condition, was positively correlated with frequency of headache and anxiety levels, and showed a negative correlation with the outcome of headache after two months treatment follow-up.

Conclusions: In migraine patients, the cortical elaboration of pain seemed not to be conditioned by verbal suggestion. The cortical zones involved in the orienting attention toward a salient painful stimulus increased their activation after the warning of reduced stimulus intensity. This rigid pattern of pain-related cortical hyper-attention appeared a negative feature for migraine severity outcome.

ScS2-11

Self-management makes sense in migraine attack prophylaxis

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Background and aims: Behavioral training (BT) can support the prevention of migraine attacks according to evidence-based treatment guidelines, and remains to be effective when offered in home-based or minimal contact settings. A self-management format of BT was shown to be feasible and efficacious when provided by supervised lay trainers. Recently a SMT application for full delivery through internet was developed in the Netherlands to increase the SMT outreach.

Methods: SMT focuses on

(1) detection of premonitory symptoms and triggers of migraine attacks and

(2) use of physiological relaxation and cognitive-behavioral self-regulation in - particularly - the premonitory stage of the attack.

SMT employs the majority of defined behaviour change techniques such as setting graded tasks, provision of behavioural models and feedback, and prompting of, respectively, self-monitoring, goal-setting, self-encouragement, practice, and planning of relapse prevention. SMT was tested in a randomized controlled trial (RCT) with >100 patients and 13 lay trainers.

Results: SMT significantly reduced attack frequency at 6-months follow-up (mean reduction: 23% with 42% responders who improved >50%; effect size: 0.6) and strongly reinforced perceived control over attack prevention. The internet application is feasible and was very well conceived by patients, their organisation, and headache specialists and is currently under test in a new RCT in The Netherlands.

Conclusion: SMT is a promising addition to non-pharmacological support in headache care.

ScS2-12

5-htr1F agonists inhibit nociceptive transmission at the trigeminocervical complex

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Background and aims: Serotonin (5-HT)1F receptor agonists, such as lasmiditan (COL-144), have been developed as nonvasoconstrictor treatments of migraine. We examined whether the selective 5-HT1F receptor agonist LY344864 has central antinociceptive actions and compared these with those of alniditan, a 5-HT1B/1D receptor specific agonist with clinical efficacy.

Methods: Activity of trigeminal nucleus caudalis (TNC) neurons (n = 15 in 9 rats) responding to mechanical stimulation of cutaneous receptive fields (RF) of the ophthalmic trigeminal division and to electrical stimulation of the middle meningeal artery and periarterial dura mater (MMA) was recorded. We examined the effect of direct microiontophoretic application of LY344864 and alniditan onto second order TNC afferents activated by glutamate.

Results: LY344864 inhibited glutamate-evoked activity with an effect that plateaued at 82 ± 3% inhibition at
20-40 nA (P < 0.001). LY344864 inhibited MMA and RF stimulus-evoked activity by some 30% and 70%, respectively, at 40 nA (P < 0.05). Alniditan inhibited glutamate evoked activity with a 95 ± 3% inhibition at 10-20 nA (P < 0.001). Alniditan inhibited both MMA and RF stimulus-evoked TCC activity at 20 nA (P < 0.05, 50%). The inhibitory effect appeared additive because the 5-HT1B/7 receptor antagonist GR127935 (40 nA) partially reversed the combined effect of LY344864 (5 nA) and alniditan (5 nA).

Conclusions: LY344864 inhibited nociceptive transmission in the rat TNC in a manner similar to triptans. The data are consistent with a central nervous system effect of 5-HT1F receptor agonists that may explain in part their clinical effect.

ScS2-13
Effects of indomethacin, naproxen and ibuprofen on no-induced trigeminal firing recorded in the trigeminocervical complex
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Background an aims: Indomethacin can be shown to alter uniquely NO-induced dural vasodilation, an effect not seen with naproxen or ibuprofen. We used a model of trigeminovascular nociceptive activation in combination with an intra-arterially administered NO-donor to study the effects of indomethacin, naproxen and ibuprofen on dural nociceptive inputs to the trigeminocervical complex (TCC) with emphasis on their specific action on NO-induced mechanisms.

Methods: Male Sprague Dawley rats (n=24) were anesthetized with pentobarbitone and cannulated for further anesthesia, physiological monitoring and drug administration. After surgical preparation trigemino-cervical wide-dynamic-range neurons, responding to electrical stimulation of the dura mater adjacent to the middle meningeal artery, were identified and recorded using electrophysiological techniques. The effect of indomethacin (5mg/kg-1), naproxen (30mg-1kg) and ibuprofen (30mg-1kg) on cell firing induced by repeated intra-arterial infusion of the NO-donor sodium nitroprusside was then tested.

Results: The infusion of SNP increased the firing rate of the tested cells (t23=8.78; P < 0.001) by 26±3% of baseline firing. Intravenous administration of control, naproxen or ibuprofen did not alter the activity in response to SNP infusions (N per group=6; P ≥ 0.33). Indomethacin significantly altered TCC activity induced by SNP infusion (F4,20=3.19, P < 0.05). Compared to baseline responses the firing rate was reduced by 28±9.8% when tested after a five-minute infusion of SNP, ten minutes post drug injection (t5=2.87; P < 0.05).

Conclusions: These experiments demonstrate for the first time an exclusive ability of indomethacin over naproxen and ibuprofen to inhibit NO-induced cell firing at the level of TCC.

Oral Presentations

OP1-1
A follow-up of the migraine with aura genome-wide association study findings
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In a recently published genome-wide association study of migraine with aura (MA) by the International Headache Genetics Consortium, we reported the first gene locus associated to common migraine. Encouraged by the result we have expanded the study aiming to find more associated loci. This should provide us deeper understanding of cellular pathways involved in migraine predisposition. Here, we report findings of follow-up studies of suggestive association signals identified in the original MA study. Genetic variants which provided suggestive association with migraine in the original study were genotyped in additional patient collections, including a clinic-based study sample from Spain (n=900, studied by individual variant genotyping) and a population-based study sample from Norway (n=1,800, evaluated in genome-wide association study data). The variants were analysed for association with both migraine with and migraine without aura using standard statistical methods. We successfully replicated several of the reported associations, leading to the identification of additional migraine gene loci. These new gene associations will likely shed more light on the pathophysiology of migraine.
OP1-2
Increased signal-to-noise in the sensory cortex after spreading depression: a possible mechanism for altered sensory perception in migraine
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Background and aims: Migraine aura is thought to be due to the passage of cortical spreading depression (CSD) through susceptible cortex. In addition to aura symptoms, migraine is characterized by alterations in sensory perception, which have in common an uncomfortable amplification of the percept. We evaluated the ability of CSD to shape subsequent cortical sensory processing.

Methods: We measured spontaneous and forepaw- and hindpaw-evoked sensory cortex activity in rat, before and after CSD, using multi-electrode array recordings and two-dimensional optical spectroscopy.

Results: Multi-electrode arrays revealed a global decrease in the amplitude and frequency of spontaneous activity after CSD, which lasted approximately one hour. In contrast, paw stimulation evoked both increases and decreases in field potential amplitude over the same time course. Increases in amplitude were at the center of evoked forepaw and hindpaw sensory maps, while decreases occurred in surround regions, with a resultant sharpening of receptive fields. The persistent, anatomically specific increase in evoked potential amplitude within sensory maps had the characteristics of long-term potentiation. Hemodynamic maps showed a sharpening of receptive fields similar to multi-electrode array data, but with amplitude decreased in both center and surround regions. Neurovascular coupling was altered throughout. Both electrophysiological and hemodynamic signal-to-noise were increased after CSD, due to increased evoked potential amplitudes, sharpened evoked potential and hemodynamic receptive fields, and globally decreased baseline noise.

Conclusions: The combination of decreased baseline activity combined with a spatially sharpened and potentiated cortical sensory response is suggestive of the alterations in sensory perception reported during migraine.

OP1-3
Trigger factors for familial hemiplegic migraine
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Background and aims: The aim was to identify and describe trigger factors for migraine in patients with familial hemiplegic migraine (FHM) from a population-based sample.

Methods: 127 FHM patients from a Danish population based cohort were sent a questionnaire listing 16 trigger factors. Distinction was made between attacks of hemiplegic migraine (HM) as well as migraine attacks with or without aura (MA/MO) within each patient.

Results: The questionnaire was returned by 75 FHM patients of whom 57 (76 %) had current HM attacks. In total 63 % (47/75) of patients reported at least one factor triggering their HM, and 36 % (27/75) were aware of at least one factor often or always giving rise to an attack of HM. Twenty per cent (15/75) reported only attacks of HM whereas FHM in combinations with MA and MO were reported by 80 % (60/75). Stress (following stress), bright light, stress (during stress), intense emotional influences and sleeping too much or too little were the trigger factors mentioned by most. The number of trigger factors did not differ between FHM patients with coexisting migraine compared to the pure FHM phenotype, nor between patents with identified mutations and no mutations.

Conclusion: Many FHM patients report trigger factors and 36% reported at least one trigger factor often or always triggering FHM. The typical triggers are the same as for MA. Patients should be educated to avoid these factors. The role of trigger factors in the onset of new or first attacks of FHM remains unknown.

OP1-4
Migraine and vascular disease biomarkers. A population-based study
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Background/aims: Migraine is a risk factor for stroke. A small clinic-based study of premenopausal women demonstrated biomarkers of endothelial activation were associated with high frequency (mean 12/mo) migraine. Our aim was to evaluate the migraine-biomarker association in a well-characterized general population.

Methods: Participants (300 women, 117 men) were from the CAMERA Study: ages 30-60 years (mean 48 yrs), 155 migraine with aura (MA), 128 migraine without aura (MO), and 134 controls. Plasma samples were analyzed for fibrinogen, Factor II, D-dimer, hsCRP, and von Willebrand factor (vWF) antigen and antibody. We compared levels of the control group to the migraine group, stratifying first by subtype and attack frequency, then by sex.

Results: In unadjusted logistic regression analyses, using controls as reference, persons with MA had increased risk (OR, 95%CI) of elevated fibrinogen (1.97, 1.23-3.16), Factor II (2.03, 1.26-3.25), and hsCRP (1.74, 1.09-2.78). All biomarkers but Factor II correlated with years and with average number of aura (but not headache) attacks (p < .001). Adjusted analyses, stratified by sex, showed that in women fibrinogen (2.98, 1.31-6.8), Factor II (3.32, 1.44-7.67), and hsCRP (3.10, 1.25-7.7) were associated with MA, >1 attack/mo, and Factor II (2.63, 1.20-5.75) with MO, <1 attack/mo. In men fibrinogen (5.89, 1.42-24.46) and hsCRP (4.72, 1.20-18.56) were associated with MO, <1 attack/mo, but 95% CI were wide.

Conclusions: Biomarkers of hypercoagulability and inflammation were associated with migraine, particularly in women, and influenced by MA and high attack/aura frequency. Whether biomarkers are associated with MRI findings remains to be determined.

PhD Thesis – Clinical

PhDTC1-1

Increase in migraine prevalence in the Danish adult population

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Background and aims: It is uncertain whether migraine prevalence has increased in modern society. Our aim was to assess any change in migraine prevalence over an 8 year period among the young adult population in Denmark.

Methods: In 1994 and 2002 questionnaires including validated questions to diagnose migraine were sent to more than 30,000 twin individuals residing in Denmark. The twins are representative of the Danish population with regard to migraine and other somatic diseases.

Results: The lifetime prevalence was 16.1% in 1994 (aged 12-41) and 25.2% in 2002 (aged 20-71). The lifetime prevalence for age 20-41 was increased from 1994 to 2002 (18.5% vs. 24.5%) by 32.2% (95% CI: 27.0-37.3%; p < 0.001). The 1-year prevalence in 2002 was 12.3% for migraine, 4.1% for migraine with aura and 8.2% for migraine without aura. The 8-year period cumulative incidence rate was 0.141 corresponding to an annual incidence rate of migraine of 17.6 per 1000 person years. We did not find significant differences in incidence between ten years age groups in the ages 20-49, however, a significantly higher incidence was found in the group aged 20-29 than 40-49 (p = 0.0007).

Conclusion: Lifetime prevalence of migraine in Denmark increased substantially from 1994 to 2002. Part of the increase may be due to increased medical consultation resulting in an increased rate of physician diagnosis or more awareness due to previously participation in the 1994 survey. It is pertinent to study the environmental causes of the increase and to implement preventive measures.

PhDTC1-2

Distinct regional grey matter volume reduction in different states of disease in cluster headache

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Objective: To identify grey matter changes in episodic and chronic cluster headache.

Background: Cluster headache(CH) usually follows a distinct course of disease with pain free episodes (outside bout), periods with headache attacks (inside bout) and chronic CH (CCH) course. A pivotal role of the hypothalamus in the pathophysiology of CH was suggested, but data are controversial.
Design/methods: We investigated 77 CH patients (19 episodic CH (ECH) inside bout, 39 ECH outside bout and 19 CCH) and 69 age and gender matched healthy controls using MRI based Voxel Based Morphometry (VBM).

Results: GM loss in major parts of the central pain network (e.g. S1, S2, thalamus, insular cortex, amygdala) was found. The hippocampal area and the cingulate cortex showed more pronounced GM volume loss in patients recently suffered from headache attacks (inside bout ECH+CCH). This was most pronounced in patients with chronic course of disease. Other regions did not show this dynamic but could be found nearly constantly over all subgroups. No changes in the hypothalamic region were found.

Conclusions: Our findings showed grey matter loss within the central pain network in CH, most pronounced in the chronic subtype but no changes in the hypothalamic area. Similar grey matter changes were observed in other chronic pain disorders. As there are more pronounced changes in inside bout and in CCH patients grey matter changes in CH are presumably partly reversible but longitudinal trials will be needed to confirm this hypothesis. The role of the hypothalamus in CH has to be discussed again.

PhDTC1-3
TREX1-mutation associated with endothelial dysfunction in RVCL patients
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Background: Retinal Vasculopathy with Cerebral Leukodystrophy (RVCL), caused by TREX1 mutation, is a macroangiopathy characterized by retinal vasculopathy, migraine, cerebral infarcts, pseudotumor cerebri, dementia, Raynaud’s phenomenon and liver and kidney dysfunction.

Objectives: To investigate vascular function at different levels of the vascular bed in RVCL patients.

Methods: Flow Mediated Dilatation (FMD) to test endothelial function of conduit arteries, Pulse Wave Analysis (PWA) and Pulse Wave Velocity (PWV) to test systemic vascular stiffness and capsaicin induced Dermal Blood Flow (DBF) to test cutaneous vascular responsiveness. RVCL patients were compared with matched healthy volunteers and Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) patients as a positive microangiopathy group.

Results: FMD of the brachial artery averaged (±SEM) 2.3%±1.1% in RVCL patients (n=10), 3.8%±1.1% in CADASIL (n=10) and 5.8%±0.9% in healthy controls (n=14) (ANOVA, p=0.05). After correction for shear rate and blood viscosity, and shear stress, FMD remained significantly (p=0.03) reduced in RVCL (3.3%±2.1%) compared to controls (10.1%±1.8%). PWA resulted in an augmentation index corrected for heart rate of 21.0%±3.2% in RVCL, 24.5%±3.8% in CADASIL and 15.9%±3.3% in controls (ANOVA p=0.05). General linear regression showed population differences (adj.R²=53%, p < 0.00001) when corrected for gender, age and blood pressure. PWV and DBF did not significantly differ between groups. However, final analysis of CADASIL data is in progress.

Conclusions: This is the first study showing decreased endothelial function of the brachial artery in RVCL, a monogenic microangiopathy disorder with migraine as one of the clinical features. Final analysis is presented at the meeting.

PhDTC1-4
Role for voltage gated calcium channels in calcitonin gene-related peptide release in the rat trigeminovascular system
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Background and aim: Voltage gated calcium channels (VGCCs) are located presynaptically on the neurons and are involved in the release of peptides. We examined the presence and importance of VGCCs in controlling the CGRP release from trigeminovascular system of rat.

Methods: We studied the effect of VGCCs P/Q-, N-, L- and T-type blockers on potassium induced CGRP release in dura mater, trigeminal ganglion (TG) and trigeminal nucleus caudalis (TNC). The released CGRP was measured by enzyme immunoassay. We also investigated the
mRNA expression of VGCC in the tissues by reverse transcription polymerase chain reaction (RT-PCR).

**Results:** Each of the four VGCCs P/Q-, N-, L-, and T-type are abundantly found in TG and TNC relative to the dura mater and each mediated a significant fraction of potassium induced CGRP release. In dura mater, blockade of P/Q-, N- and L-type VGCC significantly decreased the potassium induced CGRP release by \( \alpha \)-agatoxin TK (21%), \( \alpha \)-conotoxin GVIA (24%) and nimodipine (43%) \( \mu \)M respectively. In the TG, \( \alpha \)-conotoxin GVIA (27%) inhibited the potassium induced CGRP release significantly. In the TNC only the cocktail of blockers could reduce the potassium induced CGRP release significantly (44%).

**Conclusion:** We found expression of VGCC mRNA in dura mater, TG and TNC. In the dura mater CGRP release was blocked by all four blockers. In the TG only the N-type blocker was effective. In the TNC no blocker alone was effective, but cocktail of four blockers significantly reduced CGRP release probably indicates compensatory mechanisms from the non-blocked channels.

**PhDTCI-5**

**The evolving genetic and pathophysiological spectrum of migraine**

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**Aim:** Several genetic approaches of both monogenic familial hemiplegic migraine (FHM) and other monogenic diseases in which migraine is prevalent (e.g. retinal vasculopathy with cerebral leukoencephalopathy (RVCL)), as well as common migraine were used to identify and characterize novel migraine gene mutations and pathways.

**Methods:** Molecular genetic methods were used to identify gene mutations in genes relevant for hemiplegic migraine and other monogenic migraine-related disorders. Neurobiological methods were used to investigate functional consequences of these gene mutations. Migraine pathways were further investigated by expression profiling in brains of transgenic FHM1 mice. Finally, a genome-wide association (GWA) approach was used to investigate common migraine in migraine cohorts.

**Results:** Several novel gene mutations with clear functional consequences were identified in familial and sporadic HM patients as well as patients with other monogenic migraine disorders in which migraine is prevalent. Functional studies also included expression profiling of brains of FHM1 mice, which revealed rather stable expression profiles in the cortex, but differentially expressed neurotransmitter-related pathways in the cerebellum of FHM1 mice, that also suffer from cerebellar ataxia. Finally, a SNP affecting expression of MTDH was identified in common migraine using a GWAS.

**Conclusions:** The genetic spectrum of FHM mutations and their associated clinical features was further expanded by studies in my thesis. The first genetic variant for common migraine was identified, hinting towards gluta-mate as an important player in the pathophysiology also of common migraine. This knowledge may further increase our insight in the genetic and pathophysiological background of migraine.

**PhDTCI-6**

**Right-to-left shunts in migraine and their relationship with cerebral infarcts and white matter lesions. Results from the population based camera study**

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**Objective:** The mechanism linking migraine with aura and ischemic brain lesions remains largely unknown. We investigated the relationship between right-to-left shunts (RLS) and brain infarcts and white matter lesions (WML) in migraineurs and controls.

**Design, setting and patients:** CAMERA-2 study, a population based study of 166 migraineurs (mean age 56 y. SD 7.7, 70% female, 96 Migraine with aura) and 69 controls (55 y. SD 7.6, 65% F)

**Main outcome measures:** Presence of whole brain and posterior circulation territory (PCT) infarcts, deep white matter lesions (DWML), and infratentorial hyperintense lesions (IHL) identified on MRI scans. RLS detected by Transcranial Doppler with air contrast during normal breathing and after provocation by Valsalva maneuver. Analyses were controlled for age, sex and cardiovascular risk factors.

**Results:** Subjects with a RLS had a PCT infarct more often than those without a RLS. This association was strongest in those with a spontaneous moderate-to-large (type-I)
RLS, as they had a PCT infarct in 13% compared to 5% in those without RLS (OR 3.9, 95%CI 1.1-14.6). Type-1 RLS was also associated with IHLs (OR 2.5, 95%CI 1.0-6.4). Migraine (subgroups) did not influence these associations. In migraineurs with a type-1 RLS a PCT infarct was found in 11% vs. 6% in those without RLS (OR 2.5, 95%CI 0.4-13.5). No associations were found between RLS and DWML.

Conclusion: A moderate-to-large RLS is an independent risk factor for PCT brain infarcts and IHLs.

Late Breaking Oral Presentations

LBOP1-1
Role of 5-ht1B, 5-ht1D and 5-ht1F receptors in controlling the release of calcitonin gene-related peptide and their mRNA expression in the rat trigemino-sensory system

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Background and Aim: Triptans, a family of 5-hydroxytryptamine 1B, 1D and 1F agonists are used in the acute treatment of migraine attacks. The location and which 5-HT1 receptor subtypes mediate the antimigraine effect have still to be identified. Here we investigate the role of the 5-HT1B, 1D and 1F receptor subtypes in controlling the release of calcitonin gene-related peptide (CGRP) in dura mater, trigeminal ganglion (TG) and trigeminal nucleus caudalis (TNC). Furthermore, the mRNA expression of these receptors has been studied in the trigemino-sensory system of the rat.

Experimental Approach: A high potassium concentration was used to release CGRP from dura mater, TG and TNC. The amount of CGRP release was measured by an enzyme-linked immunoassay. The mRNA was quantified by qPCR.

Key Results: Sumatriptan significantly inhibited the CGRP release by 31% in dura, 44% in TG and 56% in TNC and it was reversed by a 5-HT1B/D/F antagonist (GR127395). The 5-HT1F agonist (LY 344864) was effective in the dura mater (26%), and the 5-HT1D agonist (PNU 142633) had significant effect in the TNC (48%), whereas the 5-HT1B agonist (CP 94253) was unable to block the CGRP release. The mRNA transcripts of all the three 5-HT1 receptor subtypes were detected in the trigemino-sensory system.

Conclusions and implications: We found that sumatriptan blocked the CGRP release via activation of different 5-HT1 receptor subtypes in peripheral and central terminals of the trigemino-sensory system. The 5-HT1F agonist was effective only in dura mater while the 5-HT1D agonist had effect only in the TNC.

LBOP1-2
Pathway ch-1 study: sphenopalatine ganglion (spg) stimulation for acute treatment of chronic cluster headache (cch) - initial results

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Background: The pain and autonomic symptoms of cluster headache result from activation of the trigeminal parasympathetic reflex, which is mediated through the SPG. We aimed to investigate the safety and efficacy of on-demand SPG stimulation for the acute treatment of CCH.

Methods: A multi-center, dose range finding, with a random insertion of placebo, multiple headache, acute treatment study design, has been initiated. All subjects meet the ICHD-II criteria for CCH with a minimum of 4 headaches/week and are dissatisfied with current treatments. Subjects are implanted with a miniaturized neuro-stimulator which, along with a controller, provides SPG stimulation. Prior to the randomized period, subject’s stimulation parameters are optimized in a titration period. The primary endpoint is acute pain relief by 15 minutes (drop to ‘none’ or ‘mild’ on the categorical scale). The primary safety endpoint is the device related serious adverse event (SAE) rate.

Results: Twelve subjects have been implanted with an average procedure time of 90 minutes (range 40-175...
Experienced a pain relief. Since five of the seven subjects also experienced headaches respectively and two subjects did not receive pain relief. Since five of the seven subjects also experienced a ≥ 50% reduction in headache frequency compared to baseline, a secondary frequency endpoint has been included. One additional subject’s neurostimulator migrated post-operatively and was explanted due to persistent numbness and pain, which resolved after explantation.

LBOP1-3
The non-genomic and genomic effects of 17β-estradiol on cgrp-induced relaxations in the porcine coronary artery
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The prevalence of migraine is higher in females than in males; this seems to be related to (changes in) levels of female sex hormones. Estrogen may induce short term effects on vascular tone via a non-genomic pathway, as well as long term effects via regulation of the synthesis and expression of proteins via a genomic pathway. Estrogen may modulate the vasorelaxation to Calcitonin Gene-Related Peptide (CGRP) via both these pathways. In this study we investigated the non-genomic (short term) and genomic (long term) effects of 17β-estradiol on CGRP-induced relaxations in porcine coronary arteries.

Porcine distal coronary arteries were incubated with 17β-estradiol (0.1 nM-10 μM) for 30 min (short term) and 24 h (long term) prior to constructing concentration response curves to CGRP. Experiments were performed in Mulvany Myographs

CGRP induced relaxations in all segments (Emax 77±4%, pEC50 8.7±0.1). The vehicle of 17β-estradiol had no effect. Short incubation with 17β-estradiol did not affect CGRP-induced relaxations. In contrast, long term incubation with 1 nM 17β-estradiol significantly reduced the Emax of CGRP (60±7%) compared with the control.

In conclusion, 17β-estradiol affects CGRP-induced relaxations in porcine coronary arteries at concentration in the physiological range. This may be an effect of 17β-estradiol on the receptor synthesis or expression via the genomic pathway. To further investigate this, analyses with biochemical techniques are now in preparation.

LBOP1-4
Evidence for a novel migraine susceptibility locus on chromosome Xq12 in a large pedigree from the genetic isolate of norfolk island
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Previous linkage studies in our laboratory have identified migraine susceptibility loci on chromosome Xq27 and Xq28. The present study continues this line of investigation by performing a complete X chromosome scan of a very large migraine pedigree from the genetically isolated population of Norfolk Island.

A novel pedigree-based association approach incorporating logistic regression was employed to analyse X chromosome-wide SNP data (15,154 SNPs). Data was ascertained for n=288 related individuals comprising a large core-pedigree of the Norfolk population. This pedigree is comprised of 76 individuals affected with IHS-diagnosed migraine (MO n=25 and MA n=51). All SNPs were ranked based on P-values adjusted for the effects of relatedness, gender and age.

SNP prioritization showed that the top 25 SNPs contained 13 SNPs localized to previously identified loci on Xq27 and 28, adding further support to the involvement of these genomic regions in migraine. In addition, 10 of the 25 top ranked SNPs mapped to a new 377Kb locus at Xq12 - strongest SNP association P=9.67x10^-5. Haplotype analysis of this new region highlighted the presence of 2 major haplotype blocks each containing a haplotype that was significantly over-represented in the migraineurs compared to controls (P<0.0005).

In conclusion, we have provided strong evidence supporting the presence of a novel migraine susceptibility locus on Xq12 in a large pedigree from the isolated population of Norfolk Island. Investigations are now underway examining these Xq12 haplotypes in unrelated case-control populations to determine whether this locus is unique to Norfolk or influences migraine susceptibility more generally.

LBOP1-5
Drd2 polymorphism is highly associated with hormonally modulated migraine
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Migraine is a disabling, highly prevalent syndromic disorder. The migraine syndrome is a complex trait in that multiple genetic loci contribute to an individual’s propensity to have recurrent migraine attacks. The weak association seen in many published genetic studies so far stems from the genetic heterogeneity of the common forms of migraine. We propose that more clearly defining the clinical phenotype of migraine will help better elucidate the genetic component involved. For example, one of the most common, definable, migraine subpopulations is menstrually related migraine which occurs at a self reported rate of about 60% of all female migraineurs. To investigate the genetic factors involved in this subpopulation we have selected 47 single nucleotide polymorphisms (SNPs), from a pathway-related group of genes involved in the hypothalamic-pituitary-gonadal-axis (HPGA) as well as those that have been implicated in previous studies to confer migraine susceptibility. Among 1393 subjects, (827 female migraine cases, 349 female controls, and 217 male controls), we found a COMT gene SNP to be associated with migraine (OR=0.72, p=0.03). Also, among 829 female migraine cases (of which 460 have hormonally modulated migraine), we found nitric oxide synthase 3 gene and dopamine receptor D2 gene SNPs to be associated with hormonally modulated migraine (OR=0.65, p=0.02; OR=0.66, p=0.006; respectively), and an endothelin receptor type B gene SNP to be associated with migraine that is not hormonally modulated (OR=1.56, p=0.002). This is the first study to find a genotype phenotype correlation in one of the common forms of migraine (hormonally modulated migraine).

Update on New Clinical Trial Data

UNCT1-1

Effectiveness of manual therapy for chronic tension-type headache: results of a pragmatic, randomised, clinical trial

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Objective: To evaluate the effectiveness of manual therapy (MT) in participants with chronic tension-type headache (CTTH)

Subjects and methods: We conducted a multicentre, pragmatic, randomised, clinical trial with partly blinded outcome assessment. Eighty-two participants with CTTH were randomly assigned to MT or to usual care by the general practitioner (GP). Primary outcome measures were frequency of headache and use of medication. Secondary outcome measures were severity of headache, disability and cervical function.

Results: After 8 weeks (n=80) and 26 weeks (n=75), a significantly larger reduction of headache frequency was found for the MT group (mean difference at 8 weeks, -6.4 days; 95% CI -8.3 to -4.5; effect size, 1.6). Disability and cervical function showed significant differences in favour of the MT group at 8 weeks but were not significantly different at 26 weeks.

Conclusion: Manual therapy is more effective than usual GP care in the short- and longer term in reducing symptoms of CTTH.

UNCT1-2

Patient-preference as primary endpoint in a randomised, double-blind, cross-over trial, comparing rizatriptan 10 mg and ibuprofen 400 mg for acute migraine treatment

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Background: The recommended primary endpoint for acute migraine trials is “the 2hr pain-free rate after treating a single attack in a parallel-group design”. When comparing established treatments, the clinical validity of this study design, however, seems limited. Cross-over trials, in which patients express a preference after exposure to both treatments, might better detect clinically meaningful differences.

Design: In a randomised double-blind, double-dummy, cross-over clinical trial, triptan-naïve patients treated three attacks with rizatriptan 10mg(R) and three attacks with ibuprofen 400mg(I). The primary endpoint was patient-preference on a 10cm scale from -5 to +5 indicating direction and strength of preference for R or I.

Results: Of the 29 subjects completing the trial (one withdrew for study-unrelated reasons), ten(34.5%)
expressed a strong to very strong preference for R and six (20.7%) for I (p = 0.15); 13 (44.8%) expressed either no (n = 4) or only a slight to moderate preference (n = 9) for either agent. The overall preference score was 0.62 ± 0.59 (SD) in favour of R (p = 0.219). High MIDAS baseline disability predicted preference for R (p = 0.039). The 2hr pain-free rates were 23/71 (32%) for R versus 9/59 (15%) for I (p = 0.03) for all moderate or severe attacks. The correlation of the individual 2hr pain-free responses with preference was modest (r = 0.64).

Conclusion: Over half of the patients expressed a clear preference for one of both treatments, which was correlated only moderately to individual 2hr pain-free responses. High baseline disability predicted preference for rizatriptan. Multi-attack, cross-over, patient-preference trials may better detect clinically meaningful treatment differences for individual patients than traditional single-attack, single-endpoint, parallel-group trials.

UNCT1-3

Efficacy and tolerability of rizatriptan in pediatric migraineurs: results from a randomized, double-blind, placebo-controlled trial using a novel enrichment design

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Background and aims: It has been difficult to establish the efficacy of acute migraine treatments in pediatric migraineurs. We evaluated rizatriptan versus placebo in pediatric migraineurs in a trial using a novel double-blind run-in enrichment design.

Methods: Randomized, double-blind, placebo-controlled, parallel-group trial in migraineurs 12-17y who had not, historically, achieved satisfactory response to NSAIDs/acetaminophen. In the Stage-1 run-in, patients were randomized 20:1 to placebo:rizatriptan. Rizatriptan dosing was weight-based (<40 kg = 5 mg, ≥40 kg = 10 mg). Patients treated within 30-minutes of a moderate/severe migraine. After 15-minutes, patients with mild/no pain (responders) took no further study medication. Patients with moderate/severe pain (non-responders) took study medication in Stage-2; those previously on placebo were randomized 1:1 to rizatriptan:placebo; those previously on rizatriptan received placebo. The efficacy analysis included only placebo non-responders in Stage-1 who were randomized to Stage-2; migraine intensity at 15-minutes post Stage-1 dose was used as Stage-2 baseline. The safety analysis included data from both stages.

Results: 702 patients treated, with 570 evaluable for efficacy. For the primary 2h pain-freedom endpoint, rizatriptan was superior to placebo: 87/284 (30.6%) versus 63/286 (22.0%), odds ratio = 1.55 [95% CI: 1.06, 2.26], p = 0.025. For 2h pain-relief, the difference directionally favored rizatriptan versus placebo, but was not significant: 167/284 (58.8%) versus 147/286 (51.4%), odds ratio = 1.35 [95% CI: 0.96, 1.90], p = 0.080. The incidences of adverse events within 14-days were similar between rizatriptan and placebo: 81/337 (24.0%) versus 83/365 (22.7%).

Conclusions: Rizatriptan was effective in eliminating pain and generally well-tolerated in migraineurs 12-17y. The double-blind run-in enrichment design likely contributed to demonstrating a significant treatment difference in pain-freedom.

UNCT1-4

Onabotulinumtoxin a for treatment of chronic migraine (cm): analysis of the preempt chronic migraine subgroup with and without prior migraine prophylactic treatment

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Background/objective: CM is a prevalent, disabling, undertreated neurological disorder. Many CM patients have tried and failed prophylactic therapy. The efficacy of onabotulinumtoxinA (BOTOX®) in CM patients with/without prior first-line migraine prophylactic treatment defined by the British Association for the Study of Headache (BASH) is reported.

Methods: PREEMPT (two phase 3 studies: 24-week, double-blind, placebo-controlled, parallel-group phase, followed by 32-week, open-label phase) evaluated efficacy and safety of onabotulinumtoxinA in CM (≥15 days/month with headache lasting 4 hours/day or longer). Subjects (n = 1384) were randomized (1:1) to onabotulinumtoxinA (n = 688) or placebo (n = 696) every 12 weeks. A post-hoc analysis categorized subjects as yes/no to prior first-line migraine prophylactic medication using the BASH guideline. Multiple headache symptom measures were analyzed.
Results: Only 41.5% (n=575) of enrolled subjects had history of prior BASH first-line migraine prophylactic medication use; most common was amitriptyline (n=337) and propranolol (n=280). Significant improvements from baseline favoring onabotulinumtoxinA over placebo were observed at Week 24 for headache days, migraine/probable migraine days, moderate/severe headache days, total cumulative hours of headache on headache days, and ≥50% improvement from baseline in headache days in both subgroups (p≤0.006). There were statistically significant improvements from baseline favoring onabotulinumtoxinA over placebo at Week 24 for patient-reported disability (HIT-6) and quality of life measures (MSQ) in both subgroups (p≤0.006).

Conclusion: OnabotulinumtoxinA is an effective treatment for CM patients who previously failed BASH first-line migraine prophylactic medications and those naïve to BASH first-line migraine prophylactic treatment.


Supported by: Allergan, Inc.

NECT1-5

A randomized, double-blind, placebo-controlled clinical trial of adding propranolol to topiramate in subjects with suboptimal response to topiramate alone


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Objective: Assess the efficacy and safety of propranolol added to topiramate in subjects with chronic migraine (CM) not adequately controlled with topiramate alone.

Background: Topiramate alone may not provide adequate control in all patients with CM. No randomized, controlled trials have assessed the value of frequently used combination preventive agents for CM inadequately controlled with one agent.

Design/methods: Double-blind, placebo-controlled randomized clinical trial conducted through the NINDS Clinical Research Collaboration, expected to randomize 250 subjects with CM not adequately controlled (≥10 headaches/month) with topiramate (50-100mg/day) to either the addition of propranolol LA (up to 240 mg/day) or placebo. Primary outcome was reduction in 28-day moderate to severe headache rate during weeks 16-24 compared to a four-week baseline (weeks -4-0).

Results: The data and safety monitoring board (DSMB), after review of an interim analysis of 171 subjects randomized by 48 sites, determined it would be highly unlikely for the combination (topiramate and propranolol) to result in a significant reduction in headache days compared to topiramate alone if all 250 participants were enrolled. The reduction in severe headache days and total headache days for combination therapy versus topiramate alone was 4.4 versus 4.7 days (moderate to severe headache days) and 6.4 versus 6.4 days (total headache days), respectively. No safety concerns were identified. Based on these results the DSMB recommended that the trial be ended.

Conclusions: This study provides evidence that propranolol LA added to topiramate, as given in this study, is unlikely to provide additional benefit when CM is not adequately controlled with topiramate alone.

NINDS contract: HHSN265200523641C

NECT1-6

Prophylactic treatment of episodic cluster headache with an angiotensin II receptor blocker (candesartan cilexetil); a multi-national, randomized, placebo controlled parallel pilot study

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University of Science and Technology, and St. Olavs University Hospital, Trondheim, Norway

**Background and aims:** The prophylactic treatment options in cluster headache are few and often with poorly documented efficacy. Candesartan cilexetil (Atacand™), an angiotensin II receptor blocker, has been shown to prevent migraine attacks, but has not been evaluated in cluster headache. The aim of this study was to evaluate candesartan as prophylactic treatment in patients with episodic cluster headache.

**Methods:** We performed a randomized, placebo controlled, 6 centre (Norway, Denmark and Sweden) parallel trial. Patients with episodic cluster headache received placebo or 16 mg candesartan titrated to 32 mg after one week, for 3 weeks in total.

**Results:** Power calculation was for 54 patients, but recruitment issues resulted in 40 patients randomized and 32 evaluable (candesartan = 19; placebo = 13). Overall mean (±SD) number of attacks (primary endpoint) was 30±22.2 vs. 44±40.1 for candesartan and placebo respectively; p > 0.1 with Mann-Whitney test. As time effects and skewness between centres were apparent, an exact Poisson test, stratified for centre, was calculated (p < 0.0001).

**Conclusions:** Candesartan 32 mg per day appears to be effective in prophylactic treatment of episodic cluster headache. Further analyses will be presented at the meeting.

**Poster Shift I**

**PS1-1**

**Patient profiling for botox (onabotulinum toxin A) treatment for migraine: a look at white matter lesions in the MRI as a potential marker**

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**Background and aims:** Pericranial intramuscular botox (Onabotulinum toxin A, Allergan Inc.) has been shown to be effective against chronic migraine in PRIMA studies. However, with high costs per treatment and limited efficacy selection of ideal patients is pertinent but remains enigmatic. To our knowledge over 80 parameters studied could not predict success. We analysed our own patients who received botox against migraine with demographic parameters but also screening MRIs for white matter lesions (WMLs).

**Methods:** Retrospective data base analysis of 529 migraineurs who received 100 IU botox at least once in a commonly used injection schema. Responders were patients who underwent three or more treatments, non-responders only one or two. Available MRIs were analysed visually for WML on T2 (and some FLAIR) sequences in a blinded fashion by two investigators.

**Results:** 529 patients received botox at Hirslanden Headache Center from 2002 to 2009. 111 were responders. 90% of the responders were female. Responders were older than non responders. 183 had MRIs, 36 available for analysis so far. Of these 23 had WMLs (64%); a meta analysis showed 22% WMLs in migraineurs, 7% in controls. We found no posterior fossa lesions.

**Conclusions:**

1) Responders to botox tend to be female, of higher age and to have a higher frequency of WMLs.

2) No lesions in the posterior fossa was found in our limited MRI analysis.

3) Consecutive MRIs should be tested for disease modifying effect of botox in migraine.

4) More MRI data and further analyses are needed.

**PS1-2**

**The subjective quality of throbbing migraine pain as a primary percept**

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The subjective quality, or percept, of throbbing pain is common in migraine. The close association between trigeminal sensory neurons and cerebral blood vessels, the trigeminovascular unit, is indeed a central feature of the prevailing view of the pathophysiology of migraine. However, clinical evidence for throbbing pain as a primary percept, arising directly from the periodic firing of trigeminovascular neurons, has been elusive. We recently examined the association between throbbing migraine pain and arterial pulse, and found that their timing and rate do not correspond. Another feature of a primary percept is that it should encode intensity, so we examined two possible scenarios in which throbbing pain might encode intensity. In the first, the throbbing rate varies with intensity, and in the second, throbbing is present when the pain level reaches a threshold. Patients with a history of throbbing migraine pain prospectively recorded the incidence of their own throbbing migraine pain, noting...
both pain intensity and pulsation rate. Recorded diary information and in-laboratory monitoring confirmed previous reports that peripheral inputs can enhance or attenuate the presence of throbbing pain. However, for a given individual, there was little variation in the throbbing rate despite their presence at a variety of different pain levels, being absent at other times when the pain was of higher intensity. We conclude that because the throbbing percept does not encode intensity it is unlikely to be a primary percept, and hypothesize that the throbbing percept is an emergent property of central processing.

**PS1-3**

Does single cortical spreading depression elicit pain behaviour in freely moving rats?

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Introduction: Behavioural animal studies are critical, particularly to translate results to human beings. Cortical spreading depression(CSD) has been implicated in migraine pathogenesis. We aimed to investigate the effects of CSD on the behaviour of freely moving rats, since available CSD models do not include awake animals.

Materials and methods: We developed a new model to induce single CSD by applying topical N-methyl-D-aspartate(NMDA) and employed a combination of an automated behavioural analysis system, video camera and ultrasonic vocalisation (USV) calls for the first time. Electrocorticograms were also studied during CSD in freely moving rats. Behaviour associated with cephalic pain was assessed in a group of rats that received sumatriptan. Cortical c-fos immunoreactivity was performed in order to confirm CSD.

Results: NMDA induced single CSD in ipsilateral cortex, evoked freezing behaviour (P < 0.01) and increased the number of wet dog shakes (WDS; P < 0.01). Grooming, locomotion, eating, drinking, and circling were not significantly altered among groups. Ultrasonic vocalisations compatible with pain calls (22.27 kHz) were only detected in 3 out of 25 rats. Sumatriptan did not significantly reduce the freezing behaviour. CSD induced significant c-fos expression in ipsilateral cerebral cortex and amygdala (P < 0.01).

Conclusions: CSD induces freezing behaviour by invoking anxiety/fear via amygdala activation in freely-moving rats. Single CSD is unlikely to lead to severe pain in freely-moving rats, though the development of mild or vague pain cannot be excluded. The relevance of rat behavioural responses triggered by CSD to migraine symptoms in humans needs further evaluation.

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**PS1-4**

The effect of mthfr c677t polymorphisms at visual evoked potentials in migraine without aura

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Background: MTHFR C677T polymorphisms is associated with mild hyperhomocysteinemia. At present time it's unclear how MTHFR C677T polymorphisms influence at migraine without aura (MwA).

Aim: The estimation of reversal-pattern visual evoked potentials (RP-VEP) in MwA in dependence with MTHFR C677T polymorphisms.

Methods: Trial was performed in 23 MwA patients. According to genetic analysis of C677T MTHFR polymorphism patients were separated into three groups: no mutation (CC, n 7), heterozygous (CT, n 10) and homozygous (TT, n 6). VEP trial was performed before genetic analysis, at the interictal period and included the record of five successive series of reversal-pattern visual stimulus.

Results: The grand average N75/P100 TT group amplitude was significantly below (6.7±2.8 mV) than CC (8.3±3.6 mV, p< 0.001) and CT (7.5±2.7 mV, p<0.01). At the same time grand average N75/P100 amplitude at CT group was significantly below (7.5±2.7) than CC (8.3±3.6 mV, p<0.02). In the TT and CT groups, mean VEP amplitude tended to be smaller than in CC in the five subsequent blocks, and it's more clear at TT group. The habituation deficit was marked in CC group (-0.12%). At the CT and TT groups the reverse dynamic was pointed (CT + 2.5%), that was reached maximum at TT group (+ 17.1%). It was shown that the difference of habituation index between CC and TT groups was significant (p=0.02).

Conclusions: The results of CT and TT migraine groups could be the confirmation of hypothesizes about mild neurotoxic effect of homocysteine and its modulating effect at serotonergic transmission.

**PS1-5**

Factors that are subjectively associated with chronification in a population of patients with moh who successfully underwent detoxification

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¹A. Sergeev, ²J. Azimova, ³E. Klimov, ⁴G. Tabeeva

Background: The estimation of reversal-pattern visual evoked potentials (RP-VEP) in MwA in dependence with MTHFR C677T polymorphisms.

Aim: The estimation of reversal-pattern visual evoked potentials (RP-VEP) in MwA in dependence with MTHFR C677T polymorphisms.

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Conclusions: The results of CT and TT migraine groups could be the confirmation of hypothesizes about mild neurotoxic effect of homocysteine and its modulating effect at serotonergic transmission.
Medication Overuse Headache (MOH) results from the chronicification of primary headaches (migraine and tension type-headache), as a consequence of the progressive increase in the intake of symptomatic drugs. The process of transformation from episodic to chronic forms is realized through a period of time of several months or years, during which an increase of attack frequency occurs. Identification of possible factors involving in this process is not easy.

We investigated the self-reported factors associated with the onset of chronic headache in the group of MOH patients of the COMOESTAS study. Of 529 eligible subjects, 495 patients (392 female and 103 males) with episodic migraine participated, 495 patients (392 female and 103 males) with episodic migraine participated. Mean age of primary headache onset was 18.02 years and 4.5 years, respectively.

At the baseline visit, the clinical interview provided data on headache history.

Patients were asked to identify self-reported factors influencing their headache pattern: stressful events (30.7%), neck traumas (4.7%), menopause (2.2%), undergoing surgery (1%), hypertension (0.6%), others (i.e. intake of oral contraceptive, 2.2%). 287 patients (58%) didn’t identify any possible factor associated with the worsening of the disease.

Chronification of primary headache is complex and involves multiple risk factors, whose identification should halt the progression of the disease. Moreover, the subjective identification is not easy and an appropriate training of these patients is needed to improve the management of this disabling disorder.

**PS1-6**

Headache and prolonged dilatation of the middle meningeal artery but not of the middle cerebral artery by pacap38 in healthy volunteers

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**Background and aims:** Pituitary adenylate cyclase-activating polypeptide-38 (PACAP38) triggers delayed migraine-like headache and marked vasodilatation in controls and migraine in sufferers. To explore a possible relationship between vasodilatation and delayed headache we examined the effect of PACAP38 on the middle meningeal artery (MMA) and middle cerebral artery (MCA) using high resolution magnetic resonance angiography (MRA).

**Methods:** In a double-blind, randomized, placebo-controlled study 14 healthy volunteers were scanned repeatedly during the immediate (0-120 min) and the delayed (2-5 h) phases after infusion of 10 pmol/kg/min PACAP38 or placebo for 20 min. Four subjects reporting delayed headache with intensity ≥ 2 (0-10 verbal rating scale) were scanned following subcutaneous administration of sumatriptan (6 mg). MRA data were assessed by a blind observer.

**Results:** We found significant dilatation of MMA (p = 0.00001), but not of MCA (p = 0.50) after PACAP38 infusion. There was no change after placebo (p > 0.40). Vasodilatation (range 16-23 %) lasted more than 5 h. The area under the curve for MMA circumference was significantly larger after PACAP38 than after placebo (p = 0.03). Sumatriptan selectively contracted the MMA by 12.3% (p = 0.043) and relieved the head pain.

**Conclusion:** The delayed headache induced by PACAP38 infusion is associated with prolonged dilatation of the MMA but not of the MCA. Sumatriptan relieves headache in parallel with contraction of the MMA but not of MCA.

**PS1-7**

Neurosteroids act through gaba-a receptors to enhance cortical spreading depression

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Cortical spreading depression (CSD) is a propagating wave of depolarization that migrates across the cortex and is implicated in the pathophysiology of migraine attacks occurring with aura. Migraine in women has long been known to be affected by changes in hormone levels. While research has focused on peripheral sources of hormones the role of recently discovered brain derived hormones (neurosteroids) remains unknown. In this study, we tested how neurosteroids influence cortical excitability and CSD by using a combined electrophysiological and intrinsic optical signal (IOS) imaging approach in rat neocortical slices. CSD was routinely induced by local application of KCl and recorded as a large transient inward current electrophysiologically and optically as a propagating wave of increased IOS. Following bath application of the neurosteroid allopregnanolone or ganaxolone both the CSD inward current and IOS signal were increased. Interestingly, neurosteroids also lowered the threshold for CSD as sub-threshold durations of KCl application that failed to induce CSD under control were dramatically transformed into CSD waves following treatment. A similar transformation was observed by raising cortical excitability with increased extracellular KCl (to 4 or 8 mM) or low concentrations of the K+ channel blocker 4-AP. Neurosteroids are thought to positively modulate the inhibitory GABAergic system. However, our findings revealed a small neurosteroid mediated increase in tonic inhibition but a selective and pronounced decrease of phasic GABAergic neurotransmission. Therefore, neurosteroids may paradoxically act to facilitate and enhance CSD through increased cortical excitability resulting from a loss of inhibition.

**Methods:** Twelve healthy volunteers were randomly allocated to receive 3.5 μg/kg/min PGF2α or placebo over 25 min in a two-way cross-over study. We recorded headache intensity on a verbal rating scale, middle cerebral artery (VMCA) blood flow velocity and diameters of superficial cerebral (STA) and radial (RA) arteries.

**Results:** We found no difference in area under the curve for immediate headache (0-90 min) between PGF2α and placebo (P = 0.144). McNemar test showed no difference in incidence of immediate and delayed headache between two experimental days (P > 0.05). There was no difference in the VMCA (P = 0.776), diameter of the STA (P = 0.460) or RA (P = 0.780) between PGF2α and placebo.

**Conclusion:** The present study demonstrates that PGF2α in contrast to vasodilating prostaglandins did not provoke headache. We suggest that vasodilating abilities of prostaglandins are important for induction of experimental headache in healthy volunteers.

**References:**

1. Ferrante, M.D. Ferrari2, M.A. van Buchem 1, M.C. Kruit1
2. E.B. Arkink1, G.G. Schoonman2, J.A. van Vliet2,3, H.S. Bakels1, M.A.M. Snoebeber1, J. Haan2,4, M.D. Ferrari2, M.A. van Buchem1, M.C. Kruit1

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**Cavernous sinus measures in trigeminal autonomic cephalalgias**

**E.B. Arkink1, G.G. Schoonman2, J.A. van Vliet2,3, H.S. Bakels1, M.A.M. Snoebeber1, J. Haan2,4, M.D. Ferrari2, M.A. van Buchem1, M.C. Kruit1**


**Background:** Based on external skull measures, patients with cluster headache (CH), the main trigeminal autonomic cephalalgia (TAC), have been suggested to have a constitutional narrowness of the cavernous sinus (CS) region. This would predispose for a relative obstruction of local venous drainage that might compromise the traversing trigeminal, sympathetic and parasympathetic nerve fibres. However, CS dimensions have never been assessed with MRI.

**Methods:** High-resolution T2-weighted MRI of the CS was acquired in 25 episodic, 24 chronic and 13 probable CH patients, 8 chronic paroxysmal hemicrania patients and 22 headache-free control subjects. Fifteen different dimensions of the CS and its surrounding structures were measured in coronal and sagittal plane. Linear regression models corrected for age, gender and transcranial diameter were applied with headache side taken into account.

**Results:** The transcranial diameter at temporal fossa level (mean±SD) was larger in all TAC patients (episodic CH 147±7 mm, p=0.04; chronic CH 150±7 mm, p< 0.001; probable CH 146±5 mm, p=0.01 and chronic paroxysmal hemicrania 145±9 mm, p=0.04) compared to controls (140±8 mm). The ipsilateral supraracotid and the
contralateral inferolateral-medial CS diameter were larger in episodic CH, and the ipsilateral subcarotid CS diameter was smaller in probable CH, compared to controls (p < 0.05). Probable CH patients had a larger left-right diameter of the pituitary gland compared to controls (p < 0.05), but estimated pituitary volumes did not differ. Other measures did not differ between TAC patients and controls.

**Conclusion:** TAC patients tend to have larger skulls. No evidence for a constitutionally narrowed CS region in TACs was found.

**PSI-10**

The migraine provoking peptide cgrp does not modulate brain activity in the human visual cortex

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**Objectives:** To test the hypothesis that calcitonin-gene-related-peptide (CGRP) modulates brain activity, we investigated the effect of intravenous infusion of CGRP on brain activity in response to a visual stimulus. In addition, we examined if a possible alteration in brain activity was reversed by anti-migraine drug sumatriptan.

**Design and intervention:** 18 healthy volunteers were randomly allocated to receive infusion of 1.5 g/min CGRP (1.5 mg/min for 20 min) or placebo and in vivo activity in the visual cortex was recorded before, during and after infusion as well as after 6 mg subcutaneous sumatriptan by functional magnetic resonance imaging (3-Tesla).

**Results:** Most of the participants (77 %) reported headache after CGRP infusion. We found no changes in brain activity in response to the visual stimulus after CGRP (P = 0.12) or after placebo (P = 0.41). Sumatriptan did not affect brain activity after CGRP (P = 0.71) or after placebo (P = 0.98).

**Conclusion:** Systemic CGRP or sumatriptan have no direct effects on brain activity in healthy volunteers. This suggests that both CGRP and sumatriptan exert their actions outside of the blood-brain-barrier.

**PSI-11**

The interinstitutional multidisciplinary biobank (biobim): the establishment of an italian biorepository for migraine research

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**Background and aims:** The Interinstitutional Multidisciplinary BioBank (BioBIM) is an organized collection of biological samples, which operates under the auspices of the IRCCS San Raffaele Pisana, Rome, a private Scientific Institution recognized by the Italian Minister of Health. BioBIM is organized in a large collection of healthy donors samples and pathology-based specimens. Since the validity of molecular studies using stored specimens depends on the integrity of the biological samples, pre-analytical standard operating procedures (SOPs) have been developed for whole blood, serum, EDTA and Na Citrate plasma specimens. BioBIM is fully equipped for the automation of sampling, processing, storage and tracking of biological samples and completely integrated with the diagnostic section through an informatic platform connecting the laboratory informatics with a pre-analytical robotic system. BioBIM is organized to ensure the storage of samples for 20 years and has obtained the Quality Certification according to standard UNI EN ISO 9001:2000

**Methods:** We set up a specific migraine section. We enrolled migraine patients consecutively seen at our Headache and Pain Unit from 1/1/10 to 31/12/10. Detailed information on demographics and clinical characteristics of migraine was gathered by means of face to face interviews.

**Results and conclusions:** We enrolled 408 pts. Two-hundreds-four suffered from MwA, 75 from MA and 129 from CM. Our is the first Italian migraine biobank. This will enhance the possibility of identifying hereditary factors for migraine, of investigating how genes interact with environment and of developing targeted treatments.

**PSI-12**

Rizatriptan for acute treatment of migraine in patients with unilateral cranial autonomic symptoms: a randomized, double-blind, placebo-controlled trial

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Object: To determine the response to rizatriptan in migraine patients with unilateral cranial autonomic symptoms (UAs).

Method: We carried out a randomised, double-blind, placebo-controlled, parallel group study using rizatriptan 10 mg for the acute treatment of a moderate or severe migraine attack in patients with UAs. Primary endpoints were pain freedom at 2 h and total migraine freedom at 2 h.

Results: 80 patients were randomly assigned to receive rizatriptan (n=41) or placebo (n=39). Rizatriptan was more effective than placebo for pain freedom at 2 h (54% vs 8%) (p<0.001) and total migraine freedom at 2 h (51% vs 8%) (p<0.001). Active treatment was also more effective than placebo for pain freedom at 1.5 h, total migraine freedom at 1.5 h, no photophobia/no phonophobia at 1.5 and 2 h, no nausea at 2 h, 2-24 h sustained pain relief and 2-24 h sustained pain freedom. Recurrence rate in the rizatriptan group was 19.5%. Rizatriptan and placebo showed a similar incidence of AEs (12% vs 10%).

Conclusions: When previously reported data for general migraine population are considered, our results indicate that patients with UAs respond better to rizatriptan 10 mg than other migraineurs.

PSI-13

Pharmacological characterization and expression of vip and pacap receptors in isolated cranial arteries of the rat

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Background and aims: Infusion of pituitary adenylate cyclase activating peptide-38 (PACAP-38), but not the related peptide VIP (vasoactive intestinal polypeptide) induces migraine-like attacks in migraineurs and headache in healthy volunteers. The aim of this study was to elucidate the vascular distribution and contribution of each of the involved receptors.

Methods: Relaxant effects of VIP, PACAP-27 and PACAP-38 were examined by wire myography on isolated middle cerebral artery (MCA), basilar artery (BA) and middle meningeal artery (MMA) of the rat in combination with specific receptor antagonists. Perfusion myography was employed to determine the effect of intraluminal versus extraluminal application of the peptides. Presence and localization of mRNA transcripts of the receptors were determined by in situ hybridization.

Results: In situ hybridization demonstrated the presence of all three receptors in the vascular smooth muscle cells. In wire myography, VPAC1 antagonist PG97269 demonstrated the highest efficacy for attenuating vasorelaxation induced by the agonists, while VPAC2 antagonist PG99265 only had some efficacy in the BA. In combination, the two antagonists demonstrated better effect than either alone. Agonists had no effect in the isolated MMA. Pure PAC1 agonist Maxadilan caused no detectable vasorelaxation. VIP applied luminally via perfusion myography caused no dilatation, indicating lack of endothelial involvement.

Conclusion: The higher efficacy of PACAP-38 over VIP to cause migraine-like headache is unlikely to be caused by stronger vasodilatory effects in the cerebral arteries. If the PAC1 receptor is involved in the pathophysiology of PACAP-induced headache, it is not because of direct vasodilatory action.
paracetamol, 400 mg etodolac and 800 mg etodolac, each in a 3-month period, interchangeably. Efficacy and safety analysis were done based on patients diaries.

**Results:** The results for 1000 mg parasetamol, 400 mg etodolac and 800 mg etodolac were as follows: response of headache at 2 hours 44.9%, 48.3% and 46.1%; pain-free at 2 hours 19.2%, 19.3% and 24.1%; sustained pain-free from 2 to 24 hours 34.3%, 38.3% and 41.1%; relapse rates in 2-24 hours 7.3%, 14.3% and 9.7%. There were no statistically difference between the groups regarding the headache response, pain-free, sustained pain-free and relapse rates. Drug related adverse events were noted in 8 patients with 1000 mg paracetamol, in 9 patients with 400 mg etodolac and in 9 patients for 800 mg etodolac during the study. The total number of adverse events were 40 and heartburn (n = 18) and nausea (n = 13) were the leading causes and there were no serious adverse events.

**Comment:** Our study showed that etodolac is a safe and effective alternative in migraine treatment and showed comparable efficacy to paracetamol 1000mg.

**PS1-16**

**Effect of cgrp infusion in a newly developed model of migraine in freely moving rats**

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**Background and aims:** CGRP infusion in humans provokes headache resembling spontaneous migraine, and CGRP receptor antagonists are effective against acute migraine. What is still fiercely contested is the site of action of CGRP and its receptor antagonists. We hypothesized that CGRP infusion will induce migraine like pain reflected by increase in Fos in trigeminal expression nucleus caudalis (TNC).

**Methods:** CGRP was infused in freely moving rats to circumvent factors like anaesthesia, acute surgery and severe hypotension, which confound expression of Fos. TNCs were isolated at different time points. The Fos mRNA and protein expression in TNC were analyzed by qPCR and immunohistochemistry. We also studied the mRNA expression of CGRP and its receptor component in trigemino-vascular along with different pain processing structures inside brain.

**Results:** CGRP infusion did not activate Fos in TNC neither at mRNA nor at protein level. mRNA expression profile showed that CGRP and its receptor components are widely distributed in trigeminovascular and different pain processing structures, but the expression pattern was unaffected in TNC after CGRP infusion.

**Conclusion:** In contrast to GTN infusion (unpublished data from our lab), CGRP was unable to increase the expression of Fos. Therefore, rat might not be a suitable model to study CGRP induced headache. The mRNA expression of CGRP receptors in various central pain pathways suggests that enhanced CGRP tone at the CNS level may be responsible for migraine.
**PS1-17**

**Sociodemographics and headache-related disability among persons with episodic migraine and chronic migraine by preventive medication use: results from the international burden of migraine-ii study (ibms-ii)**

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**Background and aims:** Few migraine patients are prescribed headache prophylaxis medications when many may benefit from such therapy. Our objective was to describe demographic and severity differences among persons with EM and CM by migraine preventive medication use status.

**Methods:** Prophylactic use and reasons for discontinuation were collected in IBMS-II, an international web-based cross-sectional survey of adults with migraine conducted in 2010. Descriptive analyses were conducted on demographics and headache-related disability as measured by the Migraine Disability Assessment Scale (MIDAS) stratified by preventive medication use (prior or current vs. no use) and EM or CM (defined as ICHD-2 criteria for migraine with ≥15 headache-days per month).

**Results:** 1,165 participants completed the survey. Prior or current preventive use was reported by 297/672 (44.2%) with EM and 330/493 (66.9%) with CM. Groups were generally similar in age, gender, and ethnicity; however, participants with prior or current use were more likely to have severe headache-related disability (MIDAS Grade IV) than untreated participants both for EM (31% vs. 19%; X² test for MIDAS grades, p < 0.001) and CM (87% vs. 80%, p=0.032).

**Conclusion:** A minority of persons with EM and CM received preventive treatment for migraine, though treatment rates were higher for CM. Characteristics of persons receiving preventive treatment included CM high levels of headache-related disability, suggesting that more disabled patients are selected as candidates for preventive treatment and that disability rather than headache days is the main driver of preventive medication use.

**PS1-18**

**Use of preventive medications for episodic migraine and chronic migraine: results from the international burden of migraine-ii study (ibms-ii)**

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**Background and aims:** Several classes of medications are used to prevent both EM and CM. Our objective was to characterize patterns of preventive medication use in persons with EM and CM.

**Methods:** Prophylactic use and reasons for discontinuation were collected in the International Burden of Migraine-II Study (IBMS-II), an international, web-based, cross-sectional survey of adults with migraine from 6 countries (United States, Canada, France, Great Britain, Germany, and Australia) conducted in 2010. Rates of prior or current use of each preventive medication class were stratified by EM or CM (ICHD-2 criteria for migraine with ≥15 headache days/month).

**Results:** 1,165 respondents completed the survey (672 EM; 493 CM). Participants were predominantly female and Caucasian, with mean age of 43.6. Current use was more common among CM (45%) than EM (28% p < 0.001). The mean number of preventive classes currently used was 1.2 for EM and 1.4 for CM. Rates of prior but not current use were also higher for CM (22%) than EM (16%; p=0.007). Antidepressants were used most frequently (EM 53%; CM 64%), followed by antiepileptics (EM 15%; CM 27%) and beta blockers (EM 28%; CM 19%). Rates of current use varied across countries, and was highest in Australia and lowest in the United States for CM participants.

**Conclusion:** Though rates of preventive medication use are higher for CM than EM, less than half of CM sufferers receive preventive treatment. Patients with CM tried more medications than those with EM, possibly highlighting the lack of efficacy of existing preventive medications.
PS1-19
Discontinuation of preventive treatment for episodic migraine and chronic migraine: results from the international burden of migraine-ii study (ibms-ii)


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Background and aims: Antidepressants, antiepileptic drugs, beta blockers, and calcium channel blockers are used to prevent migraine. Previous studies have found low levels of use and adherence these medications. Our objective was to describe reasons for discontinuation of oral preventive medications.

Methods: Prophylactic use and reasons for discontinuation were collected in the International Burden of Migraine-II Study (IBMS-II), an international web-based cross-sectional survey of adults with migraine conducted in 2010. Participants could select the following reasons for discontinuation: migraine improvement, lack of efficacy, side effects, or cost, or other. Analyses were stratified by EM and CM (ICHD-2 criteria for migraine with ≥15 headache days/month).

Results: 1,165 respondents completed the survey (672 EM; 493 CM). Participants were predominantly female and Caucasian, with mean age of 43.6. Current use of preventives was modest (EM 28%; CM 45%). Prior, but not current use (discontinuation of all prophylactics) was reported by 25% of EM and 42% of CM participants. The most common reasons reported were lack of efficacy (EM 37-48%, depending on class; CM 39-49%) and side effects (EM 35-50; CM 34-53%). The proportion of participants discontinuing because their headaches resolved was modest for both EM (8-14%) and CM (1-9%). High cost was reported infrequently (≤10% for all classes).

Conclusion: Discontinuation rates for preventive medications are high for EM and even higher for CM. Discontinuation is most often attributed to lack of efficacy and medication side effects. These findings indicate that there is significant unmet need for tolerable and efficacious prophylactic treatments.

PS1-20
Prophylactic headache treatment with the nti-tss dental splint

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Objective: To describe demographic information of NTI dental providers and reasons for prescribing.

Background: Due to treatment side effects, a fraction of migraine patients receive preventive therapy. The NTI dental appliance, approved in the US for the prevention of headache associated with migraine, has a favourable side effect profile. The use of this device remains limited in medical treatment algorithms.

Methods: Data was collected in the Patterns of NTI-tss Use Survey (2010), a web-based, cross-sectional survey of dental providers who had prescribed NTI splints. Descriptive analyses were conducted on provider demographics and reasons for prescribing NTIs.

Results: 587 participants completed the survey. 97% were general dentists. 86% had been in practice 10 years or more. 94% had more than one year experience prescribing the NTI. On average each participant had provided 160 NTIs. Participant responses about reasons for NTI use: 26% primarily for pain management, 17% primarily to protect the dentition, and 56% for both pain management and dentition protection. Of those dentists that used the NTI device for primary headache, 96% rated the NTI as highly effective. Reports of adverse events were seen in less than 2% of the responses.

Conclusions: A minority of persons with migraine receive preventive treatment. The NTI should be considered part of the preventive migraine therapy algorithm, as it has a low side effect profile, and favorable efficacy as reported by dental providers familiar with the device.

PS1-21
White matter lesions and headache; what are the risk factors?

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Introduction: In migraineurs, white matter lesions are 4 times more likely than non migraineurs.

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**Objective:** The objective of this study was to identify any outstanding risk factors for white matter lesions in a headache population.

**Method:** Ninety six MRI results (48 normal, and 48 with white matter lesions) were retrieved randomly from the hospital computer data documentation system. We compared age at onset of headache, age at consultation, sex, headache types (migraine and other headaches), frequency of headache (less than and more than 15 days per month), medication used for headache, medication overuse, vascular risk factors, and co morbid associated conditions. MRI data included white matter lesion load and brain localization.

**Results:** Outstanding data was that more women then men had white matter lesions, (42/48 women, 6/48 men). Forty of 48 patients (31 migraineurs, 9 other headache types) had headaches days more than 15 days per month. Patients with white matter lesions had more mood disorders, during the course of their lives (28/48 patients versus 8/48 in the normal MRI group). The most common brain localizations of white matter lesions were the frontal lobes and the parietal lobes, 43 patients had less than 8 lesions.

**Conclusion:** We propose that mood disorders might be a risk factor for white matter lesions in headache patients. women migraineurs, frequent migraine are already acknowledged as risk factors for white matter lesions.

**PSI-22**

Medical consultation and headache-impact (hit-6) among persons with chronic migraine (cm) and episodic migraine (em): results from the american migraine prevalence and prevention (ampp) study

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**Background and aims:** Inadequate or inappropriate medical consultation can be a significant barrier to effective migraine management. We sought to compare patterns of medical consultation to health care providers (HCPs) and headache-impact in persons with CM and EM.

**Methods:** Respondents to the 2009 AMPP survey, a longitudinal, population based study, who met ICHD-2 criteria for migraine were assigned to CM (≥15 headache-days/month) or EM (< 15 headache-days/month). Medical consultation was assessed by self-reported visits to HCPs/facilities for headache. Primary-care providers (PCPs) included internists and family doctors, specialists included neurologists and headache/pain-specialists. The Headache Impact Test (HIT-6) was utilized to assess headache-impact. Descriptive statistics were used to summarize data, t-tests were used to compare HIT-6 scores.

**Results:** In 2009, 27,253 questionnaires were fielded (10,270 control subjects), 20,107 returned (73.8%), 373 respondents meet criteria for CM, and 6,796 for EM. 48.5% (n=181) of CM respondents reported ≥1 visit to a HCP/facility for headache within the preceding 12 months, compared to 24.5% (n=1,662) of EM. Persons with CM were more likely to consult PCPs (CM: 34.1%, EM: 15.8%) and specialists (CM: 15.8%, EM: 5.6%) for headache. Among persons with CM, headache-impact was greater among those consulting neurologists/headache specialists (Mean HIT-6 score: 64.5 vs. 66.7 [both severe impact], p<0.05). Among EM, headache-impact was also higher for those consulting specialists (Mean HIT-6 score: 63.6 [severe impact] vs. 57.3 [substantial impact], p<0.001).

**Conclusion:** Persons with CM consulted HCPs more frequently, particularly specialists. Those who sought treatment had greater headache-impact among both CM and EM.

**PSI-23**

Chronic migraine (cm): prevalence, headache-related disability and sociodemographic factors in the us population: results from the american migraine prevalence and prevention (ampp) study

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**Background and aims:** Most international, population-based studies estimate CM prevalence ranging from 1.4% to 2.2%. We aimed to estimate the prevalence of CM in the US population, and stratify results by subgroups of sociodemographics and headache-related disability.
Methods: In 2004 surveys were mailed to a stratified sample of 120,000 US households. Headache frequency, symptoms, sociodemographics and MIDAS data were collected. Surveys were returned by 162,756 individuals aged ≥12. 28,621 persons reported severe headache. ICHD-2 migraine criteria were used to identify CM (headache frequency ≥15 headache days/month) and episodic migraine (EM) (<15 days/month). Crude and sociodemographically adjusted prevalence ratios (PRs) were generated. CM and EM groups were contrasted by MIDAS grades.

Results: 19,189 individuals (11.79%) met criteria for migraine (17.27% of females; 5.72% of males). 0.91% met criteria for CM (1.29% of females; 0.48% of males). Prevalence was highest in both sexes aged 40-49. Compared with persons aged 12-17, adjusted PRs in the 40-49 age group were as follows: females 4.71 (95% CI 3.24-6.83), males 3.31 (95% CI 1.99-5.49). Prevalence of CM was higher in African-Americans (females: 1.7%, males: 0.7%) than in Caucasians (females: 1.2%, males: 0.5%), but not after adjusting for sociodemographics. CM prevalence was inversely correlated with annual household income. Severe headache-related disability (MIDAS Grade IV) was reported by 37.97% of CM vs. 9.51% of EM.

Conclusion: Prevalence of CM was nearly 1% (0.91%) and was highest in adjusted models among females, in mid-life, and lowest income households. Severe headache-related disability was more common among persons with CM.

PS1-24

Multiple-attack efficacy and tolerability sumavel® dosepro™ (needle-free subcutaneous sumatriptan) among current triptan users


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Background and aims: A priority in managing migraine is rapid, sustained relief that allows return to normal functioning. Subcutaneous sumatriptan provides the fastest relief of all the triptans. Sumavel® DosePro™ is a needle-free, single-use, subcutaneous product that confers relief as early as 10 minutes postdose. Multiple-attack efficacy and tolerability of Sumavel® DosePro™ (needle-free subcutaneous sumatriptan) were evaluated among current triptan users.

Methods: Adults with IHS migraine treated with triptans administered Sumavel DosePro for ≤4 migraine attacks over ≤60 days in this open-label, multicenter study. Efficacy was assessed as % attacks with pain relief 15 and 30 minutes and 1, 2, and 24 hours postdose and % with sustained relief at 24 hours. Pain-free response and relief of associated symptoms were assessed. Adverse events were the primary tolerability measure.

Results: 212 patients administered Sumavel DosePro to treat 669 migraine attacks. The percentage of attacks with pain relief was 33.0% at 15 minutes, 70.1% at 30 minutes, 84.6% at 1 hour, 85.9% at 2 hours, and 81.3% at 24 hours. Sustained relief (1-24 hours) was observed in 67.4% of migraine attacks. Similar results were observed for the other efficacy measures. By-attack results were similar to those across attacks. Among those treating 4 attacks (n=113), 75.8% reported pain relief 2 hours postdose in ≥3 of 4 attacks. Mild, transient injection site reactions were the most common adverse events.

Conclusion: Sumavel DosePro was associated with rapid, sustained headache relief and was well tolerated in the treatment of multiple migraine attacks among current triptan users.

PS1-25

Current triptan users requiring a change in migraine therapy demonstrated improved treatment satisfaction and confidence after trying sumavel® dosepro™ (needle-free subcutaneous sumatriptan)


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Background and aims: Most migraine patients are dissatisfied with their medication. Rapid relief is the primary determinant of satisfaction with migraine therapy. Sumavel® DosePro™ is a needle-free, single-use, subcutaneous product that confers relief as early as 10 minutes after dosing. In this study, satisfaction and confidence with Sumavel® DosePro™ (needle-free subcutaneous sumatriptan) were evaluated among triptan users requiring a change in migraine therapy.

Design/methods: Sumavel DosePro was administered for ≤4 migraine attacks over ≤60 days by adults with migraine currently treated with triptans (any form, any dosage) in this open-label, multicenter study. At baseline and the end of treatment, satisfaction was measured with the revised Patient Perception of Migraine Questionnaire.
(PPMQ-R), and patients rated their confidence in treating migraine attacks. Results were assessed in patients with a baseline Migraine-ACT score ≤ 2, suggesting the need for a change in migraine therapy.

**Results:** Among the 90 patients requiring a change in migraine therapy and administering Sumavel DosePro for ≥ 1 migraine attack, PPMQ-R Overall Satisfaction score (transformed to a 0-100 scale) increased markedly from baseline to end of treatment (55.1 ± 23.2 versus 74.6 ± 27.7, p < 0.0001) as did PPMQ-R scores for Efficacy (52.5 ± 17.8 versus 74.8 ± 23.4, p < 0.001) and Functionality (46.2 ± 22.3 versus 71.3 ± 25.2, p < 0.001) and the percentage of patients confident or very confident in treating repeated migraine attacks with no deterioration in Tolerability (80.6 ± 14.72 versus 83.5 ± 17.66 p = 0.12).

**Conclusion:** Current triptan users requiring a change in therapy experienced a clinically and statistically significant increase in satisfaction and enhanced confidence in treatment after trying Sumavel DosePro.

**PS1-27**

**Referred pain and tenderness in relatives of patients with migraine and in healthy subjects**

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**Objective:** Migraine’s patients show increased referred pain in relation to healthy subjects. This may be due to the fact that repeated migraine attacks secondarily sensitize peripheral neurons. However, the possibility of increased myofascial vulnerability as a hereditary predisposing feature in migraine patients and their relatives cannot be discarded.

**Methods:** We examined the presence of referred pain and tenderness in the scalp and neck of 84 first-degree relatives of patients with migraine; forty-five (53.6%) of them experienced headaches and 39 (46.4%) did not. Thirty one healthy subjects whose relatives did not suffer headaches composed the control group. Presence and number of trigger and tender points were recorded in each group. Data were analyzed with χ² square test and analysis of variance.

**Results:** Referred pain, with or without associated tenderness, was found in 31 (68.9%) relatives with headache, 8 (20.5%) relatives without headache, and 3 (9.7%) control subjects (p < 0.0001). Mean number of trigger points was 3.9 ± 2, 1.9 ± 1.1 and 1.3 ± 0.6 respectively (p = 0.006). Tenderness without referred pain was found in 10 (22.2%) relatives with headache, 20 (51.3%) relatives...
without headache, and 12 (38.7%) controls (p < 0.021).
Mean number of tender points was 3.9 ± 2.6, 3.3 ± 1.7, and 2.1 ± 1.7 respectively (p = 0.032).

Conclusion: Referred pain and tenderness were highest among patients’ relatives with headache. Patterns of referred pain and tenderness among patients’ relatives without headache were intermediate between the former and controls, suggesting that some degree of myofascial vulnerability can be present among healthy relatives of migraine’s patients.

PSI-28
Lacosamide in the treatment of refractory trigeminal neuralgia: a case report
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Objective: Carbamazepine is the drug of choice for the treatment of trigeminal neuralgia (TN) but not every patient responds to or tolerate it. Lacosamide, an antiepileptic drug which is being also developed for the treatment of neuropathic pain, acts by enhancing the slow inactivation of voltage-gated sodium channels without affecting the fast inactivation mechanism. Thus, its mechanism of action is similar but not equal to the one of carbamazepine. We present three cases of refractory idiopathic trigeminal neuralgia successfully treated with lacosamide.

Case 1: 47-years old woman. She suffered TN of the left third branch. She was allergic to carbamazepine and did not improve with pregabalin, topiramate nor gabapentin. After adding lacosamide to her treatment she improved noticeably and gabapentin was withdrawn. With 250 mg/day of lacosamide she has been attack-free during 9 months. She does not report any effects.

Case 2: 57-years old man. He suffered TN of the second left branch unresponsive to carbamazepine and pregabalin. He improved after starting lacosamide and has been almost attack-free during the last two months with a daily dosage of 450 mg/day. He does not report side effects.

Case 3: 68-years old woman. She suffered TN of the second left branch which worsened with carbamazepine. When carbamazepine was progressively substituted by lacosamide she improved, and currently she has been attack-free during two months with a dose of 300 mg/day. She does not report side effects.

Conclusion: Our data suggest that lacosamide could be a valuable alternative to treat TN.

PSI-29
The prevalence of mthfr c677t polymorphism and the effects of vitamins therapy on disease disability in chinese migraineurs
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Background and aims: The roles of MTHFR C677T polymorphism and hyperhomocysteinemia in the pathogenesis of migraine remain controversial. We study the pattern of this polymorphism and examine the homocysteine-lowering effect by vitamin supplementation on migraine disability in Chinese migraineurs.

Methods: A single-centered and prospective intervention study with one-way within subjects design. The prevalence of MTHFR C677T polymorphism in local migraineurs was studied. Serum homocysteine level, migraine disability scoring and grading, headache frequency and pain intensity were compared before and after a 3-month trial of folic acid, vitamin B6 and B12 supplementation.

Results: The prevalence of MTHFR polymorphism in 31 subjects (41% CC genotype, 47% CT genotype, 12% TT genotype) was different from that in our community dwelling population. TT genotype was more prevalent in migraine with aura than migraine without aura (17% vs 6%). Vitamins reduced the serum homocysteine level (p < 0.001), MIDAS score (p = 0.001) and HIT score (p < 0.001). The reduction in headache scores translated into a decrease in MIDAS and HIT headache disability grading. CC genotype carriers showed significant homocysteine lowering (p = 0.001), MIDAS score reduction (p = 0.039) and HIT score reduction (p = 0.001) but not in TT genotype. There was a trend of decline in headache frequency (p = 0.039) and pain score (p = 0.061).

Conclusions: Vitamins therapy may be an effective prophylactic treatment. We also found that TT genotype was more prevalent in migraine with aura, associated with higher grade of migraine disability and less favourable response to vitamin therapy in Chinese migraineurs which warranted more aggressive management.

PSI-30
A long-term open-label study assessing the safety and tolerability of levadex® orally inhaled dihydroergotamine in adult migraineurs
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LEVADEX is an orally inhaled formulation of dihydroergotamine mesylate (DHE) in hydrofluoroalkane propellants delivered via the breath-actuated TEMPO® inhaler. Since the clinical safety of orally inhaled administration of DHE has not been previously established, this study was performed to assess the long term safety of LEVADEX. The safety was evaluated by adverse event reporting, laboratory tests, vital signs, physical examination, cardiopulmonary function lung capacity for diffusion of carbon monoxide and chest X-ray. This study lasted up to 52 weeks during which time subjects self-administered LEVADEX to treat acute migraines as needed. 675 subjects were enrolled to receive LEVADEX 1.0 mg (M). 217 subjects participated in an untreated control arm (C) to assess underlying variability of FEV1, DLco, ECHO and CXR. The mean age, % female, % with asthma history for the M and C groups respectively were 40/37 yrs, 91%/87% Female, and 24%/9% asthmatic. 263 M subjects and 195 C subjects completed the study with 12 months of follow-up. More than 9,500 migraines were treated with LEVADEX. There were no serious drug related adverse events reported, and no subject had significant respiratory sequelae. The most common adverse events were upper respiratory tract infection (14.6%), nausea (12.2%) and nasopharyngitis (10.5%). The incidence of abnormal tests for echocardiography, diffusion capacity and spirometry was low and similar between the M and C groups. LEVADEX was well tolerated over the course of up to 52 weeks and the oral inhalation route of administration for DHE was not associated with any unique safety risk.

PSI-31

Delta opioid receptors modulate migraine-related sensory hypersensitivity and cortical spreading depression

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Methods: Von Frey hair and tail immersion assays were used to evaluate mechanical and thermal sensitivity following nitroglycerin administration. Optical intrinsic signaling imaging with a thinned skull preparation was used to visualize cortical spreading depression in anesthetized mice. Cortical spreading depression was evoked by administration of KCl.

Results: The DOR agonists SNC80 and ARM390 significantly reduced nitroglycerin-evoked sensory hypersensitivity. SNC80 reduced the frequency of repetitive CSD events, and changed the characteristics of CSD propagation.

Conclusion: These data indicate that delta opioid receptor agonists modulate multiple basic mechanisms of migraine, and provide evidence in support of the potential of delta opioid receptor agonists as novel therapeutic agents for migraine.

PSI-32

Kynurenic acid is able to suppress cortical spreading depression and the effect size is sex hormone dependent

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Methods: Male and female adult Sprague-Dawley rats (n=8/group) received intraperitoneal injections of L-kynurenine (L-KYN, 300 mg/kg), KYNA precursor, combined (L-KYN+Prob) or not with probenecid (Prob, 200mg/kg), organic acid transporter inhibitor or NaCl. Cortical KYNA concentrations were determined by HPLC (n=7). Thirty min after ip injections, CSD were elicited by applying over the occipital cortex a cotton ball soaked with 1M KCl and recorded by DC electrocorticogram. In NaCl and L-KYN groups, supplementary females were added and CSD frequency was analyzed.
according to the ovarian cycle phases determined by vaginal smears.

**Results:** In both sexes, L-KYN+Prob and L-KYN increased cortical KYNA level. L-KYN+Prob, L-KYN and Prob decreased CSD frequency in female rats, while in males only L-KYN+Prob decreased CSD frequency. L-KYN effect on CSD frequency in females was the most potent in diestrous phase when gonadal hormone levels are low.

**Conclusion:** Kynurenine, by increasing kynurenic acid levels in cortex, could be a possible candidate for migraine with aura preventive treatment. Females, particularly in the ovarian cycle phase where they have low sex hormone levels, are more sensitive to the CSD suppressing effect of kynurenine.

**PSI-33**

**Tetrandrine attenuates nf-kb activation in glial cells of trigeminal ganglia on rat with migraine**

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Migraine is one of the most prevalent disabling nervous system diseases affecting the patients' quality of life. Glial cells are now recognized as an active participant in the initiation and maintenance of migraine, and play an important role in the regulation of neuronal function and releasing pro-inflammatory cytokines contributing to the migraine. NF-κB, a nuclear transcription factor, is the center of inflammatory response. Nitroglycerin (NTG)-induced NF-κB activation has been shown to play a critical role in the pathogenesis of migraine. Tetrandrine (Tet), a traditional Chinese herb as a calcium channel blocker and an inflammation antagonist, has been applied in the treatment of various neurologic diseases. Evidence has demonstrated tetrandrine as a potent inhibitor of NF-κB activation in cells. The present study aimed to investigate whether NF-κB activation in the satellite cells can lead to the release of inflammatory cytokines involving in the migraine and to explore the relationship between NF-κB and Tet in the pathology of migraine. Male Sprague Dawley rats received injection with nitroglycerin to introduce migraine. Immunohistochemistry, Western blot, and RT-PCR were used to determine the NF-κB levels and study the changes under basal conditions in response to tetrandrine injection. A significant increase in NF-κB activation was detected in the trigeminal ganglia of rats following injection with nitroglycerin. These results suggest that NF-κB activation in the trigeminal ganglia is implicated in the pathology of migraine, and Tet may be a novel and promising candidate for future treatment or prevention of migraine via inhibiting NF-κB activation in the trigeminal ganglia.

**PSI-34**

**Tetrandrine alleviates nitroglycerin-induced nociception via modulating s100b and erk in trigeminal ganglion of migraine rats**

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Activation and sensitization of trigeminal ganglia are implicated in the pathology of migraine. Satellite glial cells (SGCs), a specialized type of glia that ensheaths trigeminal neurons, play an essential role in peripheral sensitization. A traditional Chinese herb Tetrandrine (TET), as a calcium channel antagonist, shows inhibitory effect on glial activation in vitro and has been used in various neurologic diseases. This study aims to investigate the effect of TET on nitroglycerin (NTG)-induced trigeminal sensitization and the potential signal pathway related to SGCs activation within trigeminal ganglia in a migraine model. TET was administered in a rat model of migraine induced by NTG. We measured the trigeminal nociception using electronic von Frey and detected the intracellular calcium concentration by Fluo-3/AM, the expression and location of S100B and ERK in trigeminal ganglia and SGCs respectively by RQ-PCR and double immunofluorescence staining. While NTG-induced increased nociceptive behaviour, elevated intracellular calcium concentration and activated S100B and ERK were attenuated by pretreatment with TET in both trigeminal ganglia and SGCs in a dose-dependent manner. TET could significantly improve NTG-induced nociceptive behaviour and the beneficial effect of TET treatment could be related to the inhibition of calcium concentration and the down-regulation of S100B and ERK in trigeminal ganglia, especially in SGCs, suggesting that administration of TET may be useful in the therapy of migraine.

**PSI-35**

**Functional connectivity within default mode network in migraine patients**

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**Background:** The default mode network (DMN) putatively engages in self-referential cognition and passive mental activity mediation, both of which are considered prominent parts of pain perception. However, to our knowledge no studies to date have examined the functional connectivity within DMN in migraine sufferers.

**Methods:** We used magnetic resonance imaging (MRI) to examine 10 migraine patients without aura and 10 gender- and age-matched healthy controls. All participants firstly had a medical history taken and a physical examination performed, and then completed some questionnaires to assess their emotional states. Then we combined several MRI techniques to explore the changes in brain structures and functional connectivity of the DMN in migraine suffers comparing to controls at resting state.

**Results:** None abnormality was identified in the conventional MRI images. Using diffusion tensor imaging (DTI), we found several brain regions of significant differences between the migraine sufferers and the controls, and the lowest fractional anisotropy (FA) of the DMN regions appeared in the inferior temporal gyrus (ITG) and inferior parietal lobule (IPL). Using functional MRI and seed-based connectivity analyses, we found the functional connectivity was significantly decreased between bilateral IPLs in patients (p = 0.033).

**Conclusions:** Our results revealed some differences in the structure and functional connectivity within DMN between migraine sufferers and healthy controls. It suggests that parts of DMN interact with migraine pathogenesis, but whether the overlapped areas between the DMN and the pain neuromatrix or the DMN itself play a role in such disease needs further researches.

**PS1-36**

Regional brain iron levels in migraine with comorbid restless legs syndrome: a magnetic resonance relaxometry study

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**Background and aims:** An association between migraine and restless legs syndrome (RLS) has been reported but the underlying pathophysiology remains uncertain. Magnetic resonance imaging studies showed decreased levels of brain iron in RLS but increased iron deposition in migraine. This study assessed regional brain iron levels in migraine with RLS by magnetic resonance relaxometry.

**Methods:** Four groups patients or controls of similar age and sex were recruited: 22 migraineurs with RLS, 22 migraineurs without RLS, 13 primary RLS patients, and 22 normal controls. All of them received a multislice T2*-weighted gradient echo sequence for T2* relaxometry and serum ferritin level measurement. T2* relaxation time (T2*-RT) was measured in the substantia nigra, red nucleus, periaqueductal gray matter, putamen, caudate and globus pallidus. Longer T2*-RTs denote lower iron levels.

**Results:** Among these four groups, T2*-RT was significantly different in the red nucleus (migraine without RLS< migraine with RLS< primary RLS: 79.8±8.0, 85.2±9.8, 85.4±6.4, 94.4±11.5ms, p < 0.001) and substantia nigra (migraine without RLS< control< migraine with RLS< primary RLS: 77.1±8.0, 77.2±7.4, 84.1±10.7, 89.3±12.7ms p=0.001) (one-way ANOVA, post-hoc LSD test). The ferritin levels did not differ among these four groups.

**Conclusion:** Migraine was associated with higher iron levels in the red nucleus; whereas, RLS was associated with lower iron levels in both the red nucleus and substantia nigra. Compared to primary RLS, the deficiency level of regional brain iron was lower in migraine with RLS.

**PS1-37**

Oxidative stress in reversible cerebral vasoconstriction syndrome: a urine 8-iso-pgf2α study

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**Background and aims:** The pathophysiology of reversible cerebral vasoconstriction syndromes (RCVS) remains unknown. Oxidative stress is detrimental to endothelial function and vascular reactivity. We hypothesized the oxidative stress marker 8-IsopGF2α, which is also a potent vasoconstrictor, could contribute to the pathogenesis of RCVS.
Methods: We prospectively recruited RCVS patients, patients with other acute headaches, and normal controls from the headache clinic or neurology wards of Taipei Veterans General Hospital. Subjects received complete clinical investigations and urine sampling (middle-stream urine) at fasting state. Urine 8-iso-PGF2α was analyzed using high performance liquid chromatography and tandem mass spectrometry.

Results: Seventy-one patients with RCVS, 39 patients with other acute headaches, and 35 normal controls finished the study. These three groups were age- and sex-matched. The urine 8-iso-PGF2α level was significantly higher in patients with RCVS in comparison with the other two groups; whereas, the level did not differ between other acute headache and control groups (0.30±0.19 vs.0.19±0.10 vs. 0.21±0.11 ng/mg creatinine, one-way ANOVA test, p=0.001). In patients with RCVS, urine 8-iso-PGF2α level was positively correlated with the number of thunderclap headaches (r=0.397, p=0.045) but negatively correlated with heart rate variability indices (SDNN: r=−0.356, p=0.013, and SDANN: r=−0.344, p=0.017). However, the severity of vasoconstrictions was not correlated with the level of urine 8-iso-PGF2α.

Conclusions: Higher urine 8-iso-PGF2α level in RCVS patients but not in patients with other acute headache indicates that acute oxidative stress could contribute to the underlying pathogenesis. Further longitudinal studies are required to explore its biological significance.

PSI-38

Headache response rates in an acute care infusion unit for primary intractable headache in children

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Objective: Evaluate the efficacy of pharmacological treatments in a pediatric acute care infusion unit for primary intractable headache in children.

Background and aims: Pediatric patients with migraines refractory to home acute treatment are usually referred to the emergency department. A pediatric acute care infusion unit was developed to treat these patients.

Methods: Retrospective analyses of 591 visits of 350 patients who received treatment in a pediatric acute care infusion unit. Intravenous combination therapy included prochlorperazine, metoclopramide, valproate sodium injection (VSI), and/or ketorolac. Associated headache characteristics, pain scores, response rates and effectiveness of therapies were reviewed.

Results: Female: male ratio was 3.24:1; mean age was 15.15 ± 2.81 years old; mean headache severity was 6.54 ± 2.52 on a 0-10 pain scale. 393 patients reported episodic headaches with baseline headache frequency of 4.48 ± 3.58. 185 patients reported chronic headaches with baseline headache frequency of 26.31 ± 5.383 patients received prochlorperazine; 223 patients received metoclopramide; 29 patients received VSI. 68% were headache free in the prochlorperazine group; 61% were headache free in the metoclopramide group; 24% were headache free in the VSI group. The mean post treatment headache severity for those patients not headache free after receiving prochlorperazine was 3.84 ± 2.00 on a 0-10 pain scale and 4.19 ± 2.51 for those who received metoclopramide.

Conclusions: A pediatric acute headache care infusion unit offers more targeted therapies to intractable pediatric headache patients. Intravenous prochlorperazine administration is more effective than metoclopramide or VSI for primary intractable headache treatment in children.

PSI-39

A study of autonomic functions and lipid profile in patients of episodic migraine from north india

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Background: Paucity of data exists regarding autonomic functions and lipid profile in migraineurs from India.

Aim: To study the autonomic functions and lipid profile in new onset migraineurs during inter-ical state.

Methods: Consecutive treatment naïve migraine patients (with and without aura) diagnosed by ICHD II criteria and a control group of normal healthy individuals were studied. Autonomic functions were assessed interictically. Patients were only allowed acute medications (NSAIDs or triptans). Sympathetic functions (handgrip test, cold pressor test, sympathetic skin response), parasympathetic functions (resting heart rate, standing to
lying Ratio, 30: 15 ratio, valsalva ratio and tachycardia ratio) and heart rate variability were studied. These were done in the same day in a single sitting. Fasting serum samples for lipid analysis included estimation of total cholesterol, LDL, HDL and triglycerides.

Results: 54 treatment naive migraine patients (with and without aura) [M:F = 38: 16; Mean age 34 ± 4.78] and 30 age-sex matched controls were studied. Only sympathetic skin response showed significant differences between cases (latency: 1.55 ± 0.08 seconds), and controls (latency: 1.44 ± 0.16 seconds) (p value -0.0004). None of the parasympathetic tests revealed any difference. Heart rate variability was abnormal in 7/54 cases compared to 0/30 in controls (p= 0.0391). Only low density lipoprotein showed significant differences being abnormal in 24/54 (in cases) and 5/30 (in controls) (p=0.020).

Conclusion: Contrary to some previous studies showing sympathetic hypofunction in migraine patients interictally, we observed sympathetic hyperfunction. Low density lipoprotein was significantly atherogenic compared to controls.

PSI-40

Painful scalp arteries in children and adolescents suffering from migraine

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Aims: Preceding studies suggest a role of scalp perivascular structures in at least a part of adults with migraine. We aimed to evaluate the presence of pressure-painful scalp arteries in children and adolescents with migraine.

Methods: Pressure-painful points on scalp arteries were searched in 130 consecutive children (6 to 12 years old, n=67) and adolescents (13 to 18 years old, n=63) affected with migraine, 89 females (F) and 41 males (M), 109 without aura (73 F) and 21 with aura (16 F), and in 35 healthy age-matched subjects.

Results: In absence of migraine we examined 76 patients: 54 (71.0%) reported one or more pressure-painful arteries, and 22 (29.0 %) none. Of the 40 children, pressure painful arteries were found in 24, compared to 30 of the 36 adolescents (significant difference, p=.025). In the 35 controls, pressure painful arteries were present only in 5 (14.3%), with a highly significant difference (p=.0001). During a migraine attack, of the 54 patients examined, 43 (79.6 %,33 F) reported one or more pressure-painful arteries and 11 (20.4 %, 8 F) none. Pressure painful arteries were found in 21 of 27 (77.8%) children and in 22 of 27 (81.5%) adolescents. The arteries most frequently involved were the frontal branch and the superficial temporal.

Conclusions: Scalp arteries are frequently painful on pressure in children and adolescents with migraine, both in absence of and during a headache. Painful arteries suggest hypersensibility of periarterial nociceptive afferents, perhaps due to the local presence of endogenous algogenic products.

PSI-41

Abnormal associative plasticity of the motor cortex in migraine without aura patients

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Background: Deficient evoked response habituation and cortical paradoxical responses to transcranial magnetic stimulation (TMS) characterize migraine between attacks. Because these immediate and longer-lasting cortical changes presumably both reflect CNS plasticity mechanisms that alter synaptic effectiveness in the stimulated cortex through short- and long-term depression (LTD) phenomena, altered functional plasticity of sensory cortices in migraine was hypothesized. In healthy subjects (HS), paired associative stimulation (PAS), in which peripheral nerve stimuli are followed by TMS of the motor cortex, may produce a long lasting excitability depression of corticospinal output neurons. We report here the effects of PAS in migraine without aura (MO) patients.

Method: Changes in motor evoked potential (MEP) amplitudes were recorded in 7 MO patients and 7 HS before and after PAS, which consisted of 90 peripheral electrical right ulnar nerve stimulation and subsequent TMS pulse over optimal site for activation of the FDI muscle with a delay of 10ms (excitability depressing).

Results: MEP amplitudes significantly decreased after PAS10ms in HS (-19%), whereas it increased in MO patients (+26%, p=0.03).

Conclusion: These results suggest interictal impairment of LTD mechanisms in migraine. Knowing that somatosensory information, such as that induced by ulnar nerve stimulation, reaches the motor cortex via corticocortical fibres from the somatosensory cortex after a relay in the ventrolateral thalamus, or via thalamocortical fibres
from the thalamus, we postulate that the impaired LTD mechanisms in migraine could be due to a deficient thalamocortical activation, as already documented in somatosensory evoked high-frequency oscillation studies.

PSI-42
Migraine associated with syncope - peculiarities of clinical manifestations
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Introduction: The estimated prevalence of migraine associated with syncope is about 40%. Clinical manifestations suggest an implication of autonomic nervous system in migraine pathogenesis with presumed sympathetic dysfunction.

The aim of the study was to determine the peculiarities of clinical manifestations in patients with migraine associated with syncope.

Material and methods: The study included 78 patients with migraine divided in two groups: 63 patients (group I) with migraine associated with vaso-vagal syncope (mean age 37.9 ± 1.7 years) and 15 patients (mean age 34.1 ± 3.2 years) with migraine without syncope (group II). The neurogenic mechanism for syncope was determined according to European guidelines for syncope management (diagnosis and treatment), 2009.

Results: Vertigo and lightheadness on rapid upright position were presented by 54 subjects (87%) from group I and 6 (40%) of group II (p < 0.001). Twenty five subjects from group I (40%) and 3 from group II (7%, p < 0.05) had hyposalivation and dry mouth. Personality anxiety trait was statistically significantly higher in group I compared with group II (58% vs. 20%, p < 0.01). There were no differences in headache characteristics like duration, character, intensity, aggravation with physical effort and associated signs.

Conclusions: A mild clinical sympathetic dysfunction can be confirmed in patients with migraine associated with syncope, which supports the efforts in studies of common mechanisms of migraine and syncope.

PSI-43
Neurotransmitters and their receptors in human and rat sphenopalatine ganglion
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Background and aims: Clinical observations and experimental studies suggest a possible role of sphenopalatine ganglia (SPG) in the pathophysiology of migraine pain. Present study was performed to examine the expression of the parasympathetic signaling transmitters and their receptors in human and rat SPG.

Methods: Indirect immunofluorescence technique was used for the demonstration of vasoactive intestinal peptide (VIP), pituitary adenylate cyclase activating peptide (PACAP), nitric oxide synthase (NOS), glutamine synthetase (GS), glial fibrillary acidic protein (GFAP), VIP and PACAP common receptors (VPAC1, VPAC2) and PACAP receptor (PAC1). Double labeling was carried out to reveal the co-localization of the neurotransmitters and their relation to the receptors.

Results: VIP immunoreactive neurons as well as fibers were frequently found in human SPG. Many, homogenously stained NOS immunoreactive neurons were found, but no NOS-positive fibers. In addition, PACAP-immunoreactivity was found in some of the neurons and in nerve fibers. Co-localization was found between VIP and NOS.

In rat VIP-, NOS- and PACAP-immunoreactivity were found in many neurons and fibers. Co-localization of PACAP and NOS was observed in neurons. PACAP-immunoreactivity was localized in close to the cell membrane, but not in the satellite glial cells.

PAC1 and VPAC1 were found in the satellite glial cells in both human and rat.

Conclusion: The trigeminal-autonomic reflex may be active in migraine and cluster headache attacks. We hypothesized that VIP, PACAP, NOS, PAC1 and VPAC1 play a role in the activation of parasympathetic cranial outflow during primary headache attacks involving the autonomic nervous system.

PSI-44
Cgrp and its receptors in the human sphenopalatine ganglion
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Background and aims: Clinical observations and experimental studies suggest a possible role of sphenopalatine ganglia (SPG) in the pathophysiology of migraine pain. Present study was performed to examine the expression of the parasympathetic signaling transmitters and their receptors in human and rat SPG.

Methods: Indirect immunofluorescence technique was used for the demonstration of vasoactive intestinal peptide (VIP), pituitary adenylate cyclase activating peptide (PACAP), nitric oxide synthase (NOS), glutamine synthetase (GS), glial fibrillary acidic protein (GFAP), VIP and PACAP common receptors (VPAC1, VPAC2) and PACAP receptor (PAC1). Double labeling was carried out to reveal the co-localization of the neurotransmitters and their relation to the receptors.

Results: VIP immunoreactive neurons as well as fibers were frequently found in human SPG. Many, homogenously stained NOS immunoreactive neurons were found, but no NOS-positive fibers. In addition, PACAP-immunoreactivity was found in some of the neurons and in nerve fibers. Co-localization was found between VIP and NOS.

In rat VIP-, NOS- and PACAP-immunoreactivity were found in many neurons and fibers. Co-localization of PACAP and NOS was observed in neurons. PACAP-immunoreactivity was localized in close to the cell membrane, but not in the satellite glial cells.

PAC1 and VPAC1 were found in the satellite glial cells in both human and rat.

Conclusion: The trigeminal-autonomic reflex may be active in migraine and cluster headache attacks. We hypothesized that VIP, PACAP, NOS, PAC1 and VPAC1 play a role in the activation of parasympathetic cranial outflow during primary headache attacks involving the autonomic nervous system.
Background and aims: Calcitonin gene-related peptide (CGRP) is a sensory neuropeptide which plays an important role in vasodilatation and pain transmission in cranio-cervical structures. The present study was designed to examine if there is CGRP and CGRP receptor components in the human sphenopalatine ganglion (SPG) in order to reveal the interaction between the sensory and parasympathetic system.

Methods: Indirect immunofluorescence technique was used for immunocytochemical demonstration of CGRP, the calcitonin like receptor (CLR), the receptor activity modifying protein 1 (RAMP1) and glial fibrillary acidic protein (GFAP). Sections were examined and images were obtained using a light- and epifluorescence microscope coupled to camera to visualize co-labeling by superimposing the digital images.

Results: CGRP immunoreactive fibers were frequently found intraganglionic in the SPG in the vicinity of neurons. CLR immunoreactivity was observed in satellite glial cells (SGC) as well as in nerve fibers but not in neurons. RAMP1 immunoreactivity was localized in many neurons and SGC. Thus, the two CGRP receptor components were found only in the SGC.

Conclusion: Clinical studies have suggested a link between the sensory trigeminal system and the parasympathetic ganglia. In cluster headache there is release of CGRP and vasoactive intestinal peptide (VIP) which suggests activation of both sensory and parasympathetic pathways. Our results suggest a possible sensory influence in the parasympathetic cranial ganglia.

PSI-45

Chronic migraine with medication overuse: how many patients need politherapy?

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Background: Few adequate trials have tested the efficacy of specific compounds in the prophylaxis of Chronic Migraine (CM). Also, there is a dearth of studies also exploring the possibility of politherapy in this form.

Aim: To evaluate the percentage of prescription of politherapy (2 or more compounds) in the prophylaxis of CM.

Patients and methods: We reviewed the clinical records of 100 patients with CM+MO according to Silberstein & Lipton criteria, and also fulfilling ICDH-II revised criteria A-C but not D for CM, i.e. also fulfilling revised criteria for MO-headache, consecutively discharged from our Headache Center.

Results: We studied 86 women and 14 men, aged 21-75 years. At discharge, 91 patients received politherapy, 9 monotherapy. Prescribed drugs were in most cases among those included in the treatment guidelines for episodic migraine; in many cases they were combined with drugs primarily indicated for other conditions (particularly for the depression and arterial hypertension). Most patients (92 patients) presented one or more comorbid condition, the most frequent being depression (55%), hypertension (22%), sleep disorders (21%), hypothyroidism (11%).

Conclusions: No guidelines exist to address the choice of prophylaxis as well to suggest politherapy in CM. Our results showed that the vast majority of CM patients discharged from a specialty unit after MO withdrawal required politherapy. They suggest that the presence of comorbid conditions may strongly influence prophylactic treatment. This report may contribute to the understanding of medical needs of patients with CM and MO, addressing further studies aimed to develop specific treatment guidelines.

PSI-46

Undertreatment in patients with primary headaches attending headache centres

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Background: Although several compounds are available to relieve attacks, and to reduce headache frequency, surveys from different countries showed that many patients do not receive adequate therapy.

Aim: To evaluate undertreatment in a sample of patients with primary headaches.

Patients and methods: Prospective survey. Diagnoses according to the ICDH-II. Past and ongoing treatments were evaluated in consecutive patients at the time of their first visit at 7 Headache Centres in Lombardy (Northern Italy). Prescription of treatments after the visit were assessed.
Results: 600 patients were enrolled (438 women, 162 men; mean age 41.7 years). Diagnoses: Migraine in 67.5%, tension-type headache in 20.6%; chronic migraine in 7.4%; cluster headache in 3.5%; other diagnoses in 3%. Treatments at first examination: 74% patients had assumed symptomatic drugs in the past; 55% were still assuming a drug for the attack; 18% of them had taken triptans; 83% had never assumed a preventive drug; 15% had assumed it in the past; 6% were still on prophylaxis. After the examination at the Centre: symptomatic drugs prescribed in 87% patients; triptans in 60%; prophylaxis prescribed in 58%; 26% patients were instructed to keep a diary card for 3 months in order to re-evaluate the need for prophylaxis during the next visit.

Conclusions: Most patients with primary headaches receive suboptimal treatments. Our results confirm the utility of Headache Centers, and also the need for developing appropriate networks to reduce undertreatment rates, to contrast the negative impact of primary headaches.

PS1-47

Three types of spreading depression waves in the folded cortex may correspond to different diagnostic forms of migraine: consequences for noninvasive therapeutic stimulations

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Cortical spreading depression (SD) causes migraine with aura. This has been first hypothesized and was later established by imaging studies showing similarities between symptomatology of migraine aura and spatio-temporal features of SD propagation. I present a pathophysiological mechanism explaining how SD waves are formed with a characteristic confined size, shape, and temporal evolution in the two-dimensional folded human cortex. The predicted patterns are in agreement with functional magnetic resonance imaging (fMRI) data of migraine with aura. The main feature of the proposed mechanism is that cortical susceptibility for SD varies with the total size of cortical tissue already invaded by SD providing a negative feedback that limits the total size of SD. The model predicts three types of SD patterns that may correspond to different diagnostic forms of migraine, such as (i) migraine without aura, (ii) migraine with aura and (iii) migraine without headache. These three patterns allow us to predict consequences for the design and application of biomedically engineered devices, such as transcranial magnetic stimulation (TMS) devices, that can be used in therapeutic approaches to intelligently target the spatio-temporal SD patterns. I present a model-based approach to design stimulation protocols that quickly revive the physiological state of the cortex while minimizing the adverse effects of stimulations.

PS1-48

Octopamine, unlike other trace amines, inhibits responses of astroglia-enriched cultures to lipopolysaccharide via a b-adrenoreceptor-mediated mechanism. Possible role of trace amines associated receptors (taars)

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Primary headache sufferers are characterized by significant high levels of the trace amines (TAs) such as octopamine, tyramine and synephrin both in plasma and in platelets, suggesting that TAs play a role in pathogenesis of migraine. Nitric oxide (NO) is known to play a crucial role in provoking a migraine painful attack. Activated astrocytes, together with microglia, are a major source of NO production in the brain. However, no information is available concerning the possible effect of TAs on NO release from astroglial cells.

We here investigated the effect of the TAs octopamine, tyramine and b-phenylethylamine (b-PEA) on the release of NO in rat astroglia-enriched cultures stimulated with the bacterial endotoxin lipopolysaccharide (LPS). Upon LPS challenge, we observed an increase of nitric oxide synthase type 2 (NOS2) mRNA and, at later times, of nitrite accumulation, an index of NO production. In rat astroglial cultures we found, by RT-PCR, detectable levels of mRNA for trace amine receptors type 3, and 8. Octopamine, at concentrations comprised between 3-30 μM, substantially inhibited the release of NO evoked by LPS. The inhibitory effect of octopamine was fully reverted by two selective b-adrenergic receptor antagonists, propranolol and metoprolol, while the b-adrenergic receptor antagonist yohimbine was ineffective. These data, consistent with a role of octopamine as glial modulator of NO production, uncover the existence of an interaction between octopamine and heterologous b-adrenergic receptors in astroglial cells. These results may have an impact in understanding mechanisms indeed involved in the pathophysiology of migraine.
PSI-49

Chronic migraine alleviation by tDCS is predicted to be associated with current flow through pain-related (sub)cortical regions

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Aims: We investigated in a double-blind sham-controlled trial the analgesic effects of a 4-week treatment of transcranial direct current stimulation (tDCS) over the primary motor cortex in chronic migraine. In addition, using a high-resolution tDCS “forward” model, we analyzed the current flow (electric field) pattern through brain regions associated with pain perception and modulation deeper than the cortical target areas.

Methods: Thirteen patients with chronic migraine were randomized to receive 10 sessions of active or sham tDCS for 20 minutes with 2 mA over a period of 4 weeks. For the tDCS “forward” model, we adapted a high-resolution individualized model for precise anatomical representation with accurate segmentation of cortical and sub-cortical structures of interest.

Results: There was a significant interaction term (time vs. group) for the main outcome and also for length of migraine episodes (ANOVA, p < 0.05 for both analyses). Post-hoc analysis showed a significant improvement in the follow-up period (after treatment) for both outcomes in the active tDCS group only. Our forward modeling studies predicted current flow in multiple areas of cortex, as well as several sub-cortical regions implicated in migraine pathophysiology. Significant electric fields were generated, not only in target cortical regions (motor and frontal cortices), but in the insula, cingulate, thalamus, and brainstem regions.

Conclusions: Our findings give preliminary evidence that patients with chronic migraine have a positive response to anodal tDCS of the primary motor cortex. It is rationale to speculate that those regions with higher electric fields will be more likely candidates for pain modulation.

PSI-50

Functional evidence for meningeal afferents innervating extracranial structures by skull penetrating collaterals

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Introduction: In primary headaches pain can spread to or may be triggered from extracranial structures like head and neck muscles. These structures come also in the field of vision as therapeutic targets. Central neurons are commonly assumed to integrate nociceptive information from intra- and extracranial structures. Here we demonstrate for the first time functional evidence for the existence of primary afferents innervating both rat meninges and extracranial tissues.

Methods: In an in vitro model axonal activity from the meningeal branch of the mandibular nerve (spinosus nerve) was recorded. Single nerve fibres were activated by electrically, mechanically and chemically stimulating receptive fields in the cranial dura mater and extracranial tissues. A similar preparation was used to provoke neuro-peptide release in the dura by chemical or electrical stimulation of the temporal muscle.

Results: Collision of action potentials evoked in periost and dura mater confirmed axon collaterals of single afferent fibres innervating the skull. Further classification revealed predominantly C-fibers, some of them encoding mechanical stimuli in the noxious range, and few fibres with conduction velocity in the A-delta range. Stimulation of the M. temporalis with capsaicin or electrical pulses provoked significant CGRP release in the meninges within the skull.

Conclusion: Provided that these findings are similar in humans, meningeal afferents with collaterals in extracranial tissues may play an important role in primary and secondary headaches. Pain spreading to extracranial structures is rather projected than referred. Extracranial therapeutic manipulations may directly target meningeal nociceptive afferents.

PSI-51

Comparative anatomy of the trigeminal nerve fibres in the middle cranial fossa and their extracranial projections in rats and humans
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Aims: Peripheral structures may be important for the origin of headaches. Using post-mortem tracing, we examined and compared the dural and extracranial projection of nerve fibres in the middle cranial fossa and their origin in rats and humans.

Methods: Skulls of adult Wistar rats were divided in the sagittal plane, the brain was removed and the dural spinous nerve was exposed. The fluorescent tracer DiI was applied either to the distal or the proximal nerve stump. The preparations were fixed in 4% PFA and incubated for 4-6 weeks at 37°C, before they were examined with a fluorescence stereomicroscope. Likewise, the spinous nerve of human skulls was dissected and its peripheral branches traced.

Results: Retrogradely traced nerve fibres of the rat spinous nerve were located in the mandibular and maxillary region of the trigeminal ganglion. Anterogradely traced fibres were seen in the dura mater following the middle meningeal artery. Part of them left the dura and passed into or through the sutures and emissary canals of the skull, thereby innervating diploe, outer periost and splenius capitis, longissimus capitis and temporalis muscle. Similarly, in the human skull nerve fibres passed from the cranial dura into diploe and periost.

Conclusion: The rat and human dura mater of the middle cranial fossa is richly innervated by nerve fibres arising from neurons in mandibular and maxillary divisions of the trigeminal ganglion. Surprisingly, a considerable portion of the nerve fibres leave the dura innervating the skull, the outer periost, the cranial neck and masticatory muscles.

PS1-52

Fibromyalgia prevalence in a tertiary headache center
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Objective: Fibromyalgia (FMS) is a common cause of headache comorbidity, specially associated with chronic headache (de Tommaso et al, 2009). We aimed to check the prevalence and features of FMS in 1200 consecutive headache outpatients came to the tertiary headache center of Bari University.

Methods: We examined the presence of FMS, according to the American College of Reumathology. Headache Diagnosis was assessed in accord to the IHCII criteria (2004). In all patients allodynia, pericranial tenderness, anxiety, depression, quality of life, fatigue and sleep disorders were assessed. In FMS patients, the invalidity caused by generalized pain was also evaluated.

Results: FMS was represented in the 22.34 % of primary headache patients, with a significant prevalence in chronic tension-type headache and chronic migraine. Migraine with aura exhibited low FMS representation, as well as cluster headache. Sleep disturbance and fatigue prevailed in FMS patients, who showed more alldynia and pericranial tenderness. Quality of life was significantly lower in FMS patients, independently from headache diagnosis. Fibromyalgia was also more severe in patients with higher MIDAS score, alldynia and pericranial tenderness.

Conclusions: Headache and FMS are mutual causes of chronicity and invalidity, which may subtend common pathophysiological basis. Their assessment appears important for a more integrated therapeutic approach.

PS1-53

A proactive approach towards migraine patients in general practice: a pragmatic randomized controlled trial
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Aim: Optimizing treatment of frequent migraine in general practice (GP) by a proactive approach, ensuring adequate management of attacks, increased use of prophylaxis, and treatment of medication overuse headache.

Methods: Cluster randomized trial, randomization by GP (31 intervention, 33 control). Participants were using ≥2 triptans per month. GPs in the intervention group received training on migraine treatment according to the GP headache guideline. They invited participants for an evaluation of their therapy. Control group continued usual care.

Primary outcome measure was Headache Impact Test (HIT-6) at 6 months with 2.3 points as clinically relevant. Possible effect modification by psychic distress (K10).

Results: We included 490 patients (233 intervention, 257 control). The consultation was attended by 192 (82%) of
the intervention patients. 41 (21%) started prophylaxis, 24 (13%) changed prophylaxis, and 27 (14%) continued current prophylaxis.

The difference in change on the HIT-6 was 0.81 (p=0.07). For patients with low psychic distress (baseline =10≤20) this was -1.51 (p=0.008), compared to 0.16 (p=0.494) for patients with increased psychic distress. In patients not using prophylaxis at baseline and ≥2 attacks per month HIT-6 improved 1.37 compared to the controls (p=0.04).

Conclusions: An educational intervention for GPs and a proactive approach of migraine patients didn’t result in a reduction of headache complaints. For patients with no prophylaxis at baseline and with ≥2 attacks per month a significant, but not clinically relevant, difference was found. New interventions should aim at this group of patients. This intervention has less effect in patients with high psychic distress.

PS1-54

The combination of asa, paracetamol and caffeine is efficacious in the treatment of severe headache attacks: results from a multicentre, randomized, double-blind, placebo-controlled study

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We investigated efficacy, safety, and tolerability of two tablets of the fixed combination of 250 mg acetylsalicylic acid (ASA) + 200 mg paracetamol + 50 mg caffeine (Thomapyrin®) in comparison to two tablets of placebo in a post-hoc analysis of a subgroup of patients who were used to treating their episodic tension-type headache or migraine attacks with non-prescription analgesics and reported a history of headache attacks characterised by at least severe pain and greatly impaired usual daily activities and treated headaches with pain intensity of at least 48 mm assessed on a 100 mm visual analogue scale and associated with greatly impaired usual daily activities. For the primary endpoint ‘time to 50 % pain relief’ in this ITT subset (n=179 patients), the fixed combination of ASA, paracetamol and caffeine was statistically significantly superior to placebo (p=0.0008). The superior efficacy of the triple combination could also be shown for all secondary endpoints such as time until reduction of pain intensity to 10 mm, weighted sum of pain intensity difference (%SPIDweighted), extent of impairment of daily activities, global assessment of efficacy. Both treatments were well tolerated. The incidence of adverse events observed was low.

The results of this post-hoc analysis demonstrate that the fixed-dose combination of ASA + paracetamol + caffeine is effective, safe and well tolerated in the treatment of severe headache.

PS1-55

Rate of systemic absorption of sumatriptan may not explain differences in headache response suggesting the potential for an additional route to the site of action

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Objective: To compare the initial pharmacokinetics with the clinical response of different sumatriptan formulations and delivery routes with emphasis on nasal delivery.

Background: Previous studies suggest that onset of effect of sumatriptan correlates with rate, not extent, of drug absorption: nasal spray being an exception. This is possibly due to the bi-phasic absorption pattern with an initial fast nasal absorption, which is not slowed by gastric stasis during migraine attacks. However, a lingual spray also showed a bi-phasic absorption pattern suggesting that fast initial rate of absorption may be insufficient to explain the rapid onset of pain relief following nasal delivery.

Methods: Published data on the initial serum concentrations at 15 minutes (corresponding well to the first peak in bi-phasic PK-curves) from nasal sumatriptan liquid spray (10&20mg), OptiNose sumatriptan nasal powder (ON 7.5/15mg), 20mg lingual spray, 6mg transdermal, 100mg tablet and 6mg SC were compared with clinical efficacy reported at different time points.

Results: Intranasal delivery in general, and ON powder in particular, seems to offer much faster initial pain relief compared to lingual spray despite very similar initial absorption profiles that are not affected by delayed gastric absorption during migraine attacks. The ON 7.5 mg sumatriptan powder produced a similar initial PK profile to 20 mg liquid nasal spray, suggesting more efficient true nasal deposition and absorption.

Conclusions: Overall, the nasal vs. non-nasal pharmacodynamic difference suggests that an additional mechanism, plausibly related to direct trigeminal nerve activity, may contribute to improving the efficacy of sumatriptan with nasal delivery.
PS1-56

Hypnic headache - a rare primary headache disorder with very good response to indomethacin. A case report

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We report the case of hypnic headache fulfilling The International Classification Headache Disorders, 2nd edition criteria. A 64-year-old woman, who suffered from dull headaches strictly during the night for a period of 5 months. Headaches began between 2 and 4 h after she fell asleep, usually between 00:30 h and 03:30 h, waking the patient from sleep. Attacks of headache lasted from 30 to 150 minutes, with a frequency usually 4 times per week. Nausea, vomiting, photophobia, phonophobia, osmophobia, dysautonomic features and focal neurological deficits had never been associated with her headaches. For correct diagnosis of HH she provided 4 week headache diary. Time of asleep, time of onset, duration, location and intensity of pain, nausea, vomiting, changes in sensitivity to sound or light, osmophobia and autonomic symptoms were monitored. Based on the above mentioned information, the final diagnosis was established during the 4 weeks follow-up visit. After the follow-up visit, the patient was started on indomethacin 50 mg b.i.d. (day 1). This treatment reduced headache frequency and also reduced pain intensity. From day 25 on she was free of hypnic headache. On day 31 we tapered the daily dose of indomethacin to 50 mg at bedtime, the patient was still without headache. On day 60 the treatment was stopped. 12 months after the follow-up visit, the patient was still headache free.

PS1-57

Migrainous aura without headache: an ictal EEG study

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Migraine is a disorder in which central nervous system dysfunction might play a pivotal role. As there are no consistent structural disturbances, clinical neurophysiology methods seem particularly suited to study its pathophysiology.

We report the case of a 53-year-old woman, with a previous history of migraine with aura, who was hospitalized for the exploration of a left clivus chordoma. Before surgery, a carotid clamping test was realized. Right carotid occlusion lead to no clinical or neurophysiological modifications. Twenty minutes after the left carotid occlusion, the patient described a typical visual aura without headache that disappeared after clamping arrest. Electroencephalographic (EEG) monitoring do not revealed EEG changes both in right and left sides. But, using the Fast Fourier Transform algorithm to analyze EEG recordings, we demonstrate that a left slow posterior activity appears in the left posterior regions five minutes before the visual aura and disappears after the disappearance of the visual aura.

This case report has two special interests: the first one is the demonstration that cortical spreading depression occurs before the clinical symptoms; the second one is the clinical validation of the Nozari’s hypothesis that demonstrate that the occurrence of cortical spreading depression appeared to be related to the magnitude and duration of flow reduction.

PS1-58

The comparable effectiveness of different medication in migraine prevention

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Background: Many medication use for migraine prophylactic but they comparable effectiveness less understood.

Aim: To determine the comparable effectiveness of different pharmacologic agent in migraine prevention in open-label study.

Methods: 62 consecutive migraine patients (according to the ICHD II) (male 5, female - 67, age from 18 to 60 years) were evaluated using visual analogue scale (VAS) and MIDAS.

Results: Mean frequency attack per month was 8.0±6.5, average attack duration 24.1±14.7 hours. Headache intensive to VAS 7.6±1.4. All patients were randomised on three groups. First group (21 patients) used propranolol (40 mg) combine with amitriptyline (25 mg). second group (22 patients) used gabapentine (900 mg), third group (17 patients) - lamotrigine (150 mg). All patients had completed a headache diary. At 90 days in first group were observed reduction of headache intensity to VAS 7.6, attack duration 14.7 hours. Headache intensity to VAS 7.6, attack duration 14.7 hours. Headache intensity to VAS 7.6, attack duration 14.7 hours.

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attack on 42.3% and MIDAS from 25.9±1.9 to 13.1±1.5 (p=0.002); in third group to VAS from 7.8±0.3 to 5.8±0.2 (p=0.0004), number attack - on 43.8% and MIDAS from 25.5±2.4 to 14.1±1.2 (p=0.003). The attack duration decrease in group gabapentine in 2.8, in group propranolol with amitriptyline in 2.1 and in group lamotrigine in 1.6 times.

**Conclusions:** The combine of propranolol with amitriptyline more effective as preventive treatment migraine for reduce of number attack, headache intensive and disability but gabapentine more successfully reduce the attack duration.

**PSI-59**

**Chronic exposure to sumatriptan, but not to sumatriptan plus naproxen, induces latent sensitization and increased excitability of dural afferents**

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Excessive use of triptans can lead to a condition known as medication-overuse headache (MOH), a significant clinical problem that often limits the utility of these drugs. The mechanisms leading to triptan-induced MOH are not completely understood. Prior studies have shown that chronic sumatriptan administration in rats produces long lasting neural adaptation and a state of latent sensitization that persists for weeks after discontinuation of the drug. This latent sensitized state is characterized by the development of cutaneous allodynia following exposure to stress or nitric oxide donors, two potential migraine triggers. We now show that latent sensitization does not occur if sumatriptan is co-administered with naproxen. A six day exposure to sumatriptan and naproxen together via osmotic minipump did not lead to development of stress or NO donor-induced cutaneous allodynia two weeks after discontinuation of the drug. In order to examine the potential mechanisms of triptan-induced latent sensitization, electrical excitability of identified dural afferent neurons was studied in vitro. Neurons taken from sumatriptan-treated rats two weeks following drug discontinuation showed increased action potential firing compared to those treated with the combination of sumatriptan and naproxen. These data provide a potential mechanism for MOH in which chronic triptan exposure leads to increased excitability of dural afferents. Further, these data suggest that the presence of naproxen protects against the triptan-induced neuronal changes that may lead to MOH.

We wish to acknowledge the generous support of GlaxoSmithKline in providing funding for these studies.

**PSI-60**

**Vip/pacap receptors in the perfused middle cerebral artery of rat**

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**Background and aims:** Vasoactive intestinal peptide (VIP) and pituitary adenylate cyclase activating peptide (PACAP) containing perivascular nerves surround cerebral vessels and originate mainly in the sphenopalatine ganglion. Clinical observations studies suggest a role of the parasympathetic system in primary headaches. Since the two peptides have potent effects we sought to examine their receptors in the perfused middle cerebral artery (MCA).

**Methods:** Indirect immunofluorescence technique was used for the demonstration of the VIP/PACAP receptors VPAC1, VPAC2 and PAC1 receptors using specific antibodies; this was confirmed by Western blot. The functional responses to VIP, PACAP27 and PACAP38 were examined in a pressurized arteriograph allowing administration of the peptides luminally and abuminally. In addition myography was used on ring segments.

**Results:** We observed immunoreactivity towards VPAC1, VPAC2 and PAC1 receptors in the MCA smooth muscle cells. In the perfusion method abuminally but not luminally applied VIP, PACAP27 and PACAP38 caused concentration-dependant relaxations of the MCA. These relaxations were inhibited by the two blockers PACAP6-38 and PG99-465. This was confirmed in vitro myography.

**Conclusion:** Clinical studies have shown that the trigeminal-autonomic reflex may be active in migraine and cluster headache attacks. We revealed that VIP and PACAP, released from the parasympathetic nerves may act on receptors located in the MCA smooth muscle cells while systemic VIP/PACAP does not act on endothelium or can pass the blood-brain barrier.

**PSI-61**

**Immunoreactivity of calcitonin gene-related peptide (cgrp) and its receptor components in human and rat spinal cord at c1-level**

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Background: Calcitonin gene-related peptide (CGRP) has a key role in migraine pathophysiology and is associated with activation of the trigeminovascular system. Some of the associated symptoms in migraine point to involvement of brain stem regions. Previously we studied CGRP signaling in the spinal trigeminal nucleus. In the present study we examined the distribution of CGRP and its receptor components at the C1-level.

Methods: Immunofluorescence method was used to study the distribution of CGRP and its receptor components- calcitonin like receptor (CLR) and receptor amplifying peptide1 (RAMP1)- in human C1 and to compare that of rat, using a set of newly characterized antibodies. Double staining with CGRP and the receptor components was performed. In addition, double stainings with CGRP, and synaptophysin (synaptic vesicles) and IB4 (C-fibers) were performed.

Results: Positive CGRP fibers were detected in laminae I and II. The CGRP staining was similar in rat, except for CGRP positive neurons found close to the central canal. CGRP and synaptophysin was detected in same laminae but in different structures. A similar finding was observed with CGRP and IB4. CLR and RAMP1 were detected in laminae I and II. However, they were not expressed in the same fibers as CGRP. In rat, the receptor components were also detected on capillaries.

Conclusion: This study demonstrates the expression of CGRP and its receptor components in C1, and for the first time indicating the possibility of CGRP signaling in the human C1. Our results suggest C1 as a possible site of action for CGRP antagonists.

PS1-62
The effectiveness of topiramate in the treatment of cervicogenic migraine (cm)
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Background and aim: The treatment of cervicogenic migraine (CM) is considered a challenge for most clinicians, as symptoms can be similar, due to its anatomic and pathophysiology complexities. Successful treatment usually requires multi-disciplinary approach. The objective of the study is to evaluate the effectiveness of Topiramate in the treatment of CM.

Method: 100 patients were evaluated according to IHS classification of secondary headaches at the Pain & Headache Center, IMC, KSA. Patients were randomly allocated to receive either Topiramate alone or in combination with Tizanidine for 6 months. Both groups were allowed to have an average of 10 sessions of physical therapy. First group (N=48) received Topiramate 50mg twice daily and Tizanidine 2mg at bedtime, while the second group (N=52) received Tizanidine 2mg only. Inclusive criteria: 38 males, 62 females; ages between 25-55 years, with a mean of 40. 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 (Topiramate and Tizanidine), and Tizanidine alone, respectively.

Conclusion: Patients receiving the combination therapy of Topiramate and Tizanidine showed more significant symptomatic improvement compared to those receiving Tizanidine alone.

PS1-63
The effectiveness of infusion therapy in the treatment of transformed migraine (tm)
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Background and aim: Transformed migraine (TM) is a chronic, daily headache, with vascular quality. It usually occurs in people during their 20s and 30s with long history of migraines. Additionally, patients usually use large doses of analgesics and experience withdrawal headaches. Our objective is to evaluate the effectiveness of infusion therapy in the treatment of TM.

Method: 40 patients were evaluated at the Pain & Headache Center, IMC, KSA according to IHS classification. Patients were requested to quit all analgesics causing TM. Patients were allocated to receive either IV infusion (N=19) or bridge therapy (N=21) as per patients’ preference. Infusion therapy (Dihydroergotamine; Valporic acid; Magnesium sulfate; Lorxicam; and Granisetron) was provided as per protocol over 3-5 days. Oral bridge therapy (Eletriptan and Etoricoxib) was administered daily for 15 days. This was followed by Topiramate 100mg daily for 6 month as a preventive therapy. Inclusive criteria: 18 males, 22 females; ages 20-50 years, with a mean of 35. Exclusive criteria: pediatrics; patients older than 50, with uncontrolled diabetes, blood pressure, other neurological deficits; or pregnancy.

Results: Average symptomatic improvement of 79%, according to numeric pain scale, was recognized in patients.
receiving infusion therapy and appreciated within one week of therapy. However, an average improvement of 60% was recognized by patients receiving oral bridge therapy and appreciated within one month of therapy.

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

**PSI-64**

**The efficacy of gliacin, a specialized boswellia serrata extract, on indomethacin responsive headache syndromes**

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**Background and aims:** Indomethacin responsive headache syndromes (IRHS) are a group of heterogeneous primary headache disorders which promptly and completely respond to indomethacin often to the exclusion of other treatments. The objective of this study was to determine the efficacy and tolerability of the nutraceutical Gliacin, a specialized *Boswellia serrata* extract (SBSE), in the treatment of a series of subjects with confirmed IRHS.

**Methods:** A total of 27 subjects with confirmed IRHS were placed on suspected therapeutic doses of SBSE. While on SBSE subjects maintained headache diaries capturing information such as headache frequency, headache severity, MIDAS, HIT-6, Headache-Related Quality of Life scores and side effects experienced. An analysis comparing SBSE and indomethacin was conducted.

**Results:** Seventy-eight percent of subjects reported over a 70% improvement with SBSE. The group’s average headache days per month were 28 prior to indomethacin, 2.3 while on indomethacin and 1.8 while on SBSE. The average pain levels (0-10) were 8.2, 2.0 and 2.3 respectively. The average HIT-6 scores were 67, 46 and 43 respectively. The average Headache Related Quality of Life scores were 56, 25 and 20 respectively. The average MIDAS scores were 80, 9, and 3 respectively. Sixty-seven percent of subjects rated their overall satisfaction and side effect level with SBSE superior to indomethacin.

**Conclusions:** Nearly 8 out of 10 subjects with an IRHS experienced a significant benefit from SBSE including decrease headache frequency, intensity and related disability. The use of SBSE in the treatment of IRHS warrants further investigation and has widespread clinical implications.

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a recent genome wide association study reported an association of rs1835740 and migraine.

**Methods:** Participants were recruited from the Danish Headache Center and from specialist practices in the periods 1999-2002 and 2005-2006, and diagnosed according to the International Classification of Headache Disorders (ICHD-II) using a validated physician conducted semi-structured interview. A large number of clinical characteristics were systematically determined. Adult Caucasians of Danish ancestry diagnosed with MA and successfully genotyped for the SNP 1835740 were included. Patients with hemiplegic migraine were excluded. Blood samples were collected for extraction of genomic DNA and genotyped for the common susceptibility variant rs1835740.

**Results:** 691 successfully genotyped MA patients with substantial description of their clinical characteristics were included. 251 were heterozygous and 40 were homozygote for the minor allele A of marker rs1835740. Carriers of the risk allele showed a non-significant tendency towards having a higher frequency of aura symptoms and a non-significant tendency towards milder migraine headache characteristics and fewer accompanying symptoms. These tendencies were not increased in homozygote carriers.

**Conclusion:** None of the clinical characteristics of migraine with aura were significantly influenced by the common susceptibility variant on 8q22.

**PS1-67**

**Elevated cardiovascular risk related cytokines in pediatric migraineurs**

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**Background and aims:** The migraine disease, especially migraine with aura, is a known risk factor for cardiovascular and cerebrovascular disease in man and women, however the exact mechanism by which migraine leads to these diseases is still unrevealed.

The aim of our study was to investigate cardiovascular risk-predicting cytokine levels in pediatric migraineurs.

**Methods:** We included 99 migraine patients (M): 16 hemiplegic migraineurs (HM), 30 migraine with aura (MA) and 53 migraine without aura (MO). The control group (C) consisted of 53 healthy volunteers. The plasma levels of the sCD40L, t-PA, MCP-1, IL-8, sP-selectin, sVCAM-1 were measured simultaneously by beads-based multiplex flow cytometric assay in the peripheral blood during the interictal phase.

**Results:** Plasma level of the sCD40L was increased in the M (p< 0.01) and HM groups (p< 0.001) compared with controls and also in the HM vs MO (p< 0.05). The t-PA plasma level was higher in the M, MO and HM patients than in the controls (p< 0.01). The sVCAM-1 concentration was elevated in all migraine subtypes (p< 0.001) and showed higher level in the HM group than in the MO patients (p< 0.01).

**Conclusions:** The elevated plasma concentrations of the cardiovascular cytokine sCD40L, t-PA and sVCAM might indicate an increased cardiovascular risk in pediatric migraineurs through altered thrombocyte function and endothelial activation. Our results suggest that the migraine related cardiovascular risk is already present in childhood.

**PS1-68**

**Visual aura rating scale applied into neurological clinical practice**

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**Background:** Transient visual symptoms are frequent in neurological practice implying a large differential diagnosis. To support the diagnosis of visual headache auras (VHA) the Visual Aura Rating Scale (VARS) was created by Eriksen to quantify the relevance of VHA cardinal features. This scale has 96% sensitivity and 98% specificity for the diagnosis of VHA in an outpatient headache clinic.

**Aims:** VARS application in a hospital based neurological practice and definition of its utility for the differential diagnosis between VHA and other visual symptoms.

**Methods:** Prospective study through VARS application to in and outpatients, as well as those observed in the emergency department, with transient visual symptoms (< 24 hours), excluding diplopia. Definitive diagnosis was established according to clinical criteria and additional diagnostic exams.

**Results:** We included 37 patients, 26 females, mean age of 38.6 years. Visual symptoms were scotomas in 16 patients, fortification spectra in 9, decreased visual acuity in 3, hemianopia in 3, metamorphopsia in 2, blurred vision in 2, hallucinations and miodesopsias in one patient each. Definitive diagnoses were primary headaches: migraine with visual aura in 24, stroke in 3, tumors in 2, epilepsy in one, ophthalmological disorders in 3 and somatization in one. VARS had a 94% specificity and 69.56% sensitivity for the diagnosis of AVE, with seven false negative results.

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Conclusions: VARS is easy to apply, useful for the diagnosis of VHA. It is very specific but not so sensible. A VARS with a negative result doesn’t allow the exclusion of the diagnosis of VHA.

PS1-69

Brain-derived neurotrophic factor is increased in migraine and cluster headache

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Background: Brain derived neurotrophic factor (BDNF) is associated with pain modulation and central sensitization. Recently, BDNF has been implicated in migraine pathophysiology due to its known interaction with calcitonin gene-related peptide. This study aimed to investigate peripheral levels of BDNF in patients with primary headaches.

Material and methods: Bi-center prospective trial enrolling 4 groups of patients: episodic migraine with and without aura, episodic cluster headache, episodic tension-type headache and healthy individuals. In migraineurs, venipuncture was performed twice: outside attacks and during typical migraine attacks prior to pain medication. In cluster headache patients serum samples were collected in- and outside bout. Analysis of BDNF was performed using enzyme-linked immunosorbent assay technique.

Results: Migraine patients (n=61) revealed significantly higher BDNF serum levels during migraine attacks (n=17) compared to headache-free intervals (n=47, p<0.01), patients with tension-type headache (n=6, p<0.001) and healthy controls (n=22, p<0.0001). Patients with cluster headache (n=64) showed significantly higher BDNF concentrations during cluster bouts (n=34) compared to healthy controls (p<0.01).

Conclusion: These results show that BDNF is increased in patients with migraine and cluster headache during migraine attacks and inside cluster bouts, respectively, and further support the role of BDNF in the pathophysiology of those headache types.

PS1-70

Changes in headache associated behaviours in rats treated with no donors

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Background: Patients suffering from primary headaches like migraine respond to nitric oxide (NO) donors with attacks or aggravation of their types of headache. Besides, weather changes (temperature, atmospheric pressure) are suggested to trigger headaches. Nausea and loss of appetite are common symptoms in migraine. The aim of this study was to examine whether NO donors and lowering barometric pressure affect behaviour, appetite and body weight of rats.

Methods: Several days after inserting a catheter into the jugular vein, either sodium nitroprusside (SNP 50 μg/kg) or saline was infused for 30 min and the spontaneous behaviour was recorded for the following two hours. Behaviour was analysed in a blinded manner from the video recordings.

In other experiments body weight and food intake were measured. Rats were deprived of food for one day before they were placed in a climate chamber and i.p. injected with 2.5 mg/kg glyceryl trinitrate (GTN) or saline. Then the barometric pressure was lowered within 8 min by 40 hPa and kept at this level for 8 min, while rats were fed ad libitum.

Results: After SNP infusion, animals showed more frequently inactive (like sleeping) and less frequently active (like sniffing) behaviours compared to saline infusion. In starved rats food intake (“appetite”) and body weight during low pressure exposure and the following day was not different between GTN injection and the vehicle injection.

Conclusion: We conclude that in rats NO donors cause a reduction in activity but not food intake as possible behavioural analogues of headache-like pathological conditions.

PS1-71

Alleviation of ‘triptan sensations’ by a kampo medicine, kakkon-to-ka-senkyu-shin’i


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**Background:** Triptan treatment of migraine attacks frequently causes unpleasant side effects such as nausea, neck and shoulder stiffness and chest pain. These side effects, which are described as ‘triptan sensations’, not only detract from triptans’ excellent effects against migraine attacks but also compel some patients to avoid these medicines completely despite their effectiveness for their migraine.

**Case report:** We report a 37 years old man with a history of migraine without aura. Sumatriptan, eletriptan and rizatriptan are very effective for his migraine attacks, but at the cost of nausea, neck stiffness and unpleasant ‘plugged’ sensations in his chest and hypochondrium. His episodes of acute sinusitis often triggered migraine attacks so poor control of his sinusitis was compounded by more frequent migraine. We prescribed kakkon-to-ka-senkyu-shin’i 7.5g/day to improve his sinusitis (this is an approved indication for kampo), simultaneously his migraine attacks also reduced in frequency. Interestingly, the simultaneous administration of triptans and kakkon-to-ka-senkyu-shin’i prevented his ‘triptan sensations’ from developing not only with sinusitis but also on occasions when he didn’t have sinusitis.

**Conclusion:** Kakkon-to-ka-senkyu-shin’i has been proved to have some pharmacological actions including muscular relaxation and blood flow amelioration in addition to its effect against sinusitis. These actions match the ‘triptan sensations’ and this medicine should promote ‘side-effect free’ treatment with triptans. Moreover, other medicines with similar actions to kakkon-to-ka-senkyu-shin’i may also reduce ‘triptan sensations’.

**PS1-72**

**Efficacy and tolerability of rizatriptan rpd 10 mg in an open label randomized trial**

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**Background:** Aim of this trial was to investigate efficacy and tolerability of rizatriptan RPD 10 mg for treatment of migraine attacks in patients with non-satisfactory response to previous pharmacologic treatments.

**Methods:** Patients were instructed to treat two migraine attacks. One attack was treated with previous medication and the second with rizatriptan in a randomized order.

**Results:** In a multicentre randomized prospective open label trial, 197 patients were included. Complete data of 95 patients were available for analysis. The primary endpoint defined as pain free two hours after intake of study medication was observed in 52.6% of the patients in the rizatriptan group compared to 36.8% in patients using previous medication ($p < .001$). Secondary endpoint was pain free after 24 hours (78.6% for rizatriptan and 61.1% (n.s.) for patients’ previous medication). Time to complete relief of any associated symptom was 729.1 minutes for treatment with rizatriptan compared to 1257.8 minutes for treatment with previous medication ($p < .0001$). Time to relief of functional impairment was also significantly ($p < .0001$) shorter for rizatriptan than for previous medication (630.7 vs 1088 minutes). Sustained pain relief 24 hours after intake of medication was achieved in 76.8% of the attacks cured with rizatriptan, while this criterion was reached in only 61.1% of the attacks cured with previous medication (n.s.). 20.8% of the patients showed adverse events after intake of both, rizatriptan and patients’ previous medication.

**Conclusion:** Rizatriptan RPD 10mg is superior to analgetics or other triptans in patients who show unsatisfactory response to these treatments.
Conclusions: Reduced acquisition of conditioned eye-blink responses suggests subclinical cerebellar dysfunction in patients with migraine. Findings were most pronounced in patients with migraine with aura. Compared to studies in patients with cerebellar diseases timing and extinction of learned responses was not disturbed.

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PSI-74
Beta-blocker migraine prophylaxis affects the excitability of the visual cortex as revealed by transcranial magnetic stimulation

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Objectives: To assess effects of beta-blocker migraine prophylaxis on cortical excitability determined by transcranial magnetic stimulation (TMS).

Methods: Phosphene and motor thresholds (PT, MT) were investigated in 29 patients with migraine, in 15 of them prior to and following preventive medication with metoprolol and in 14 patients without prophylaxis.

Results: Headache frequency significantly decreased during treatment with metoprolol compared to patients without preventive treatment ($p = 0.005$). Mean PT were significantly increased in patients with prophylaxis, but remained unchanged in patients without treatment ($51.5 \pm 7.5\%$ vs. $63.6 \pm 8.4\%$ in treated and $53.7 \pm 5.3\%$ vs. $52.3 \pm 6.3\%$ in non treated patients; $p = 0.040$). Mean MT did not significantly differ neither between groups nor before and after treatment. In the group of all patients, a significant inverse correlation between headache frequency and the level of PT was found ($R = -.629; p < 0.01$). There was, however, no significant correlation in the subgroups of preventively treated and not treated patients.

Conclusions: We conclude that

a) clinical efficacy of beta-blockers in migraine could be (at least partly) explained by effects on the excitability of the visual cortex and that

b) the PT determined by TMS appears suitable to measure migraine activity in the individual patient. This may be useful in clinical trials investigating migraine preventive drugs.

PSI-75
Epidemiology of chronic migraine: prevalence in a tertiary headache centre in germany

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Background and aims: In the 2nd edition of the International Headache Classification (ICHD-2), the concept of chronic migraine (CM) was introduced. The existence of chronic migraine as a diagnosis in itself was and still is controversially discussed. The aim of the original diagnostic criteria from 2004 was to include many of the patients seen in tertiary headache referral centres: patients with a history of migraine who experience headache more than half the time. In 2006, revised criteria were published. In this study, the prevalence of patients fulfilling the original 2004 criteria for diagnosis of chronic migraine is analysed.

Methods: The clinical database of patients treated in the Kiel Headache Centre between 2004 and 2010 was used. The prevalence of patients fulfilling diagnostic criteria for chronic migraine according to the International Headache Classification (ICHD-2) was calculated.

Results: A total data set of $n=52191$ was evaluated. The diagnosis of chronic migraine was made for $n=476$, i.e. 0.9%.

Conclusion: The diagnosis of “chronic migraine” according to the International Headache Classification (ICHD-2) is rarely made even in a tertiary headache referral centre. This form of migraine does exist, but it only represents a very small sub-group.

PSI-76
Transdermal sumatriptan for acute treatment of migraine

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Migraine is a widespread neurologic disorder characterized by episodes of headache accompanied by photophobia, phonophobia, gastrointestinal symptoms and, often, cutaneous allodynia. Presenting symptoms can vary considerably, but gastrointestinal disturbances are common. Current pharmacotherapy for migraine includes analgesics, nonsteroidal anti-inflammatory drugs, and several 5HT-agonists in various oral, nasal spray, and subcutaneous formulations. Among the 5HT-agonists, sumatriptan is the most frequently prescribed, but its therapeutic limitations
(ie, poor absorption, low bioavailability, adverse events) cause some migraineurs to delay or avoid treatment and may lead to suboptimal outcomes. Transdermal sumatriptan (Zelrix®) is a new, single-use, disposable patch that delivers sumatriptan via iontophoresis, a less invasive method for systemic delivery. Pharmacokinetic data indicate that transdermal sumatriptan delivery is fast, consistent, and predictable. Results from well-controlled clinical studies demonstrate significant superiority versus placebo within 1 hour post-activation for pain relief (P < 0.0002) and nausea-free (P < 0.0251); at 2 hours post-activation, transdermal sumatriptan significantly outperformed placebo for pain-free (P = 0.009), pain relief (P < 0.0135), photophobia-free (P = 0.0028), phonophobia-free (P = 0.0002), and migraine-free (P < 0.0135). Transdermal sumatriptan is well tolerated, and reported adverse events are mostly mild, transient application site reactions. This article reviews the evidence in support of the efficacy and safety of transdermal sumatriptan for acute treatment of migraine.

**PSI-77**

**Efficacy of topiramate in migraine prophylaxis**

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**Objective:** Topiramate, a broad-spectrum anticonvulsant with multiple mechanisms of action, may be effective in preventing migraine headaches. We report the results of retrospective chart review of patients treated with topiramate for prophylaxis of migraine.

**Methods:** To be included in the analysis, patients had to have an International Headache Society (IHS) diagnosis of migraine with or without aura and at least one follow-up visit after 4 or more weeks on topiramate were eligible: 39 patients (26 (66%) women and 13 (34%) men) aged 18 to 68 years met these criteria. All patients were examined with electroencephalography and evoked potentials (visually and somatosensory). Topiramate was initiated at 25 mg and was increased by 25 mg weekly until the target dose of 100 mg/day was achieved.

**Results:** Significant percentage reductions from baseline in 4 weeks headaches frequencies were observed among patients with moderate/severe headaches whether they were or were not taking concurrent preventive medications (30.3%; P = 0.001 and 40.2%; P = 0.02). Smaller reductions were observed in patients with mild headaches who were or were not using preventive medications concurrently (12.3% and 11.3% respectively; both decreases were not significant). The most common adverse effects were paresthesias, drowsiness, diarrhea, decreased appetite and weight loss.

**Conclusion:** Topiramate may be effective in reducing the frequency of both mild and moderate severe migraine headaches who do not respond to other treatments.

**PSI-78**

**Effectiveness of a multidisciplinary pain therapy program in headache patients**

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**Background:** In chronic back pain patients, multidisciplinary therapy approaches have been shown to reduce pain significantly compared to standard care. In contrast, only few data are available for multidisciplinary therapies in headache patients and the effectiveness of such programs has yet to be proven. Here we present the results of a multidisciplinary pain management program in patients suffering from headache involving physiotherapy, behavioural and education group therapy.

**Methods:** Sixty patients suffering from frequent headache were enrolled in a 200-hour multidisciplinary program. The efficacy of the treatment was assessed on the basis of pain intensity, headache frequency, anxiety, depression and health-related quality of life and vitality. The data were collected and statistically analysed via nonparametric tests (Friedman, Wilcoxon) at the time of enrollment, 6 and 12 months after the end of the treatment program.

**Results:** A significant reduction (p < 0.05) in headache intensity was measured 6 and 12 months after the treatment with an effect size of 0.52 and 0.49, respectively. Patients experienced fewer headache and migraine days and migraine attacks. The therapy reduced also anxiety (p = 0.018) and depression (p < 0.001) and improved the overall patient vitality (p < 0.001) with an effect size of 0.59 for vitality and 0.60 for depression. The benefit of the therapy remained stable between 6 and 12 months after treatment.

**Conclusion:** The 200-hour multidisciplinary therapy program is effective for headache patients. Clinically relevant improvements could be achieved and remained stable for at least 6 (anxiety) to 12 months after the therapy.
**PSI-79**

**Factors of risk that they can induce to the abandon of the preventive treatment of migraine**

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**Summary:** Between 30-50% of patients are non-adherents to the preventive treatment of the migraine, this process is poorly understood and risk factors have not been clearly identified.

**Aim:** To analyze some factors that can predispose to the abandon of the preventive treatment

**Patients and method:** Analysis of clinical database of patients who for the first time needed preventive treatment of his migraine, two groups was established as they had left the preventive treatment or not. There were analyzed and compared different demographic and clinical variables in both groups.

**Results:** A total of 800 patients with migraine, who for the first time needed preventive treatment, were included in the study. The percentage of patients that discontinued the preventive treatment was 19.7%. In the group that left, the variables: “age”, “number of migraine attacks before the preventive treatment” and “adverse effects” showed significant differences with those of the group of patients who did not leave the preventive treatment.

**Conclusions:** The drug used as preventive treatment, the adverse effects of the treatment, the youngest age and the minor number of attacks before the beginning of the treatment favoured the abandon of the preventive treatment.

The type of migraine (episodic or chronic), the presence of medication overuse and the acute medications used for the symptomatic treatment of the attacks they did not relate with the suspension of the preventive treatment.

**PSI-80**

**The neural basis of decision-making under risk in medication overuse headache patients: an fMRI study**

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Chronic Migraine with medication overuse shares some pathogenetic mechanism with other kinds of drug addiction. A PET study supports the link between Chronic Migraine with medication overuse and addiction in particular a persistent orbitofrontal hypofunction has been found as in drug dependence.

The abnormal activation within the neural basis of decision-making under risk seems to underlie the maladaptive behaviour of substance abuse, including impaired decision making.

We tested the hypothesis of a dysfunction of the neural circuit of decision-making under risk in Chronic Migraine with medication overuse with functional Magnetic Resonance Imaging (fMRI): 8 female patients (CM group) and 8 female control subjects (C group) were studied, during the execution of a decision utility paradigm, while subjects decided whether to accept or reject gambles that offered a 50/50 chance of either gaining one amount of money or losing another amount. We used the paradigm by Tom et al. (2007) that successfully identified a diminished neural sensitivity to losses among individuals who were less loss averse and thus more risk seeking, a feature of substance abusers.

We observed activations in the targets of the mesolimbic and mesocortical dopamine systems in both groups. Moreover CM patients showed, in comparison to C group, an hypoactivation in the ventral tegmental area (VTA) and in substantia nigra (SN) and an hyperactivation in (p < 0.001 uncorrected) in superior medial frontal gyrus.

Our results seem to support the hypothesis of a dysfunction in the neural basis of decision-making under risk in CM with medication overuse patients.

**PSI-81**

**Functional-mri (f-mri) evaluation in chronic migraine with medication overuse**

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Patients suffering from chronic migraine with medication overuse show abnormalities in personality similar to those of subjects addicted; these changes may be predictive for a therapeutic success or not. moreover some neuro-imaging
studies showed that abnormalities revealed in these patients are related to a specific cerebral pattern alterations which can return normal after withdrawal.

Aim of the study was to submit a group of chronic migraine (CM) patients with medication overuse to a functional MRI study to determine the presence of specific cerebral alterations. Data were compared with those of controls and patients suffering from chronic migraine without medication overuse. Patients with medication overuse repeated the same analysis 6 months after withdrawal.

All subjects who entered the study, were scanned on a 1.5 T MR system. All subjects were submitted to an initial psychophysical testing session.

Mechanical pressure stimuli of 3 sec in duration at the three intensity levels was performed.

f-MRI analysis showed a significant decreased activation in the right supramarginal gyrus and in the right inferior and superior parietal cortex in the chronic migraine patients pre-withdrawal compared to controls and chronic migraine without medication overuse. The hypoactivation returned to normal state 6 months after withdrawal.

f-MRI seems to be a useful technique to obtain information on particular neuronal changes of the pain network involved in this type of patients. The activated areas are congruent with some data of the literature. More subjects are needed to evaluate the possible changes after withdrawal.

PS1-82
Chronic migraine associated with arterial essential hypertension: ambulatory blood pressure monitoring results
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Objectives:
- To evaluate the circadian variation of blood pressure (BP), mean BP levels, BP loads, and BP variability in chronic migraine patients with essential arterial hypertension.

Methods: Ambulatory blood pressure monitoring was performed for ten patients with chronic migraine and arterial hypertension, selected at the Headache Center between September 2010 and February 2011. According to the recommendation of British Hypertension Society, the blood pressure thresholds while awake was consider <135/85 mmHg and while asleep < 120/70 mmHg. The data was analyzed with Epi Info package for Windows.

Results: A study sample consists of ten patients, mean age 56.8 ±6.12, predominant female. The headache history was 29.4 ± 9.7 ages and hypertension history was 10 ± 5.1 ages.

Mean blood pressure levels were: systolic 129 ± 10.86 mmHg for daytime and 118.9 ±12.03mmHg for nighttime and diastolic 81.8 ± 8.96 mmHg for daytime and 71.6± 9.10 for nighttime. The mean daytime blood pressure levels were above the proposed thresholds in 40% of the patients and nighttime levels was above the thresholds in 70% of the patients.

According to circadian variation of blood pressure 6 patients (60%) was consider non-dipper and 4 patients (40%) dipper.

Conclusion: Chronic migraine patients with associated hypertension have a high risk for cardiovascular events as they often present non-dipper status.

PS1-83
Demographic characteristics of chronic migraine patients. Results in an outpatient headache clinic
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Aims: Characterize and compare demographic profiles for patients with chronic migraine (CM) with or without medication overuse (MO), and episodic migraine.

Methods: Patients firstly attended in an outpatient headache clinic during 3 years. Demographic and nosological characteristics were gathered. Episodic migraine (Group A) was classified accordingly to ICHD-II criteria. For CM with (Group B) or without MO (Group C) we considered revised IHS criteria.

Results: 1195 patients were attended during inclusion period. 65.4% (175 males, 607 females) were diagnosed of migraine. Among them 68.1% (130 males, 403 females) were included in group A, 17.8% (23 males, 116 females) in group B, and 14.1% (22 males, 88 females) in group C. Comparing Group B with Group C, age at first visit (47.8 ± 12.9 vs. 42.1 ± 14.1 years respectively), and time from migraine onset (25.1 ± 13.1 vs. 17.3 ± 12.9 years) were significantly increased in MO patients, but there was no difference in age at onset (22.7 ± 10.9 vs. 24.6 ± 12.5 years). Percentage of patients with no...
previous preventive therapy was significantly decreased in Group B (34.3% vs 59.8%). We found no difference between Groups B and C in gender, Headache Impact Test 6 (HIT6) score (61.3 ± 6.8 vs. 60.6 ± 7.4) and patients with HIT6 score over 55 (78.6 vs 84.5%).

**Conclusion:** CM with or without MO represents a burdensome group of patients in our headache clinic. CM patients with MO were referred later, and received a poorer preventive therapy than CM without MO patients.

**PS1-84**

**The efficacy of melatonin in migraine prophylaxis**

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**Objective:** Migraine is a primary headache presenting with attacks, associated with autonomic and neurological symptoms, it is a group of syndromes. Preventive treatment with beta-blockers, antidepressants, and antiepileptics have wide range side effect profiles and new therapies are needed. In this study, we investigated the effectiveness of melatonin in migraine prophylaxis.

**Methods:** Analysis were made in 23 migraine patients. Each patient received 3 mg / day of oral melatonin tablet at night for 2 months. Compared with pre-treatment, the number of attacks per month, attack time (in hours), and VAS (Visual Analog Scale), pain intensity, the number of triptan use and analgesic use were recorded in each patient 2 months after treatment.

**Results:** 6 men, 17 women were included to the study. The mean age of patients was 32.69 ± 8.60 (18-50), respectively. The number of attacks in a month after treatment compared with pre-treatment was decreased from 6.04 ± 1.33 to 3.21 ± 1.97, the attack time was decreased from 32.52 ± 21.23 to 13.91 ± 10.99 hours, as assessed by the VAS: pain intensity was decreased from 93.91 ± 4.75 to 53.69 ± 24.82, the number of analgesics use was decreased from 6.95 ± 3.68 to 3.43 ± 2.59, the number of triptan use was decreased from 5.43 ± 1.23 to 2.52 ± 1.75. Improvements in all parameters were statistically significant (p < 0.001).

**Conclusion:** The results of the study suggests that melatonin prophylaxis may be effective in migraine and it is a safe treatment method.

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Purpose: Topiramate for the treatment of migraine prophylaxis may cause side effects such as cognitive dysfunction. In this study, it was aimed to investigate the efficacy of topiramate in migraine patients and the effect of event-related potentials and their effect on cognitive functions.

Materials and methods: In our study, 21 migraine patients (Group 1) and 21 healthy control group (Group 2) were included. In both groups, event-related potentials (P300 Latency (L), Amplitude (A) and N200 Latency (L), Amplitude (A)’s) were evaluated. 2 months after topiramate treatment in migraine group, the same parameters were evaluated again. In addition, in migraine group: the number of attacks within a month, number of painful days, VAS scores, number of analgesic use, number of triptan use were compared before treatment (BT) and 2 months after treatment (AT).

Results: Evaluation between group 1 and group 2 showed no difference (p > 0.05). Topiramate-treated Group 1’s BT and AT values were compared; all parameters of AT compared with BT were statistically significant (P < 0.05). Group 1’s number of attacks one month BT, the number of painful days in a month BT, VAS scores BT, the number of analgesic use BT, the number of triptan use BT had all decreased AT. All parameters for AT compared to BT were statistically significant (P < 0.05).

Conclusion: As a result of our study; 100 mg topiramate was effective in the treatment of migraine. However, in the process of this treatment electrophysiological studies showed that cognitive functions are also affected adversely.

PS1-87
A new dimension in cgrp homeostasis: evidence for cgrp uptake in mice vas deferens
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Background and aim: CGRP is extensively distributed in afferent nerves and capsaicin can stimulate its release from these nerves. But this phenomenon has not been investigated in-depth in isolated preparations. This study characterised the pharmacology of CGRP and explored uptake of exogenous CGRP in the mouse isolated vas deferens (MVD).

Methods: The effects of capsaicin and CGRP on electrically-evoked twitch responses of MVD were investigated in the absence or presence of CGRP receptor antagonists.

Results: Capsaicin caused a triphasic response; the first phase (1 nM-30 nM) was marked by a CGRP-dependent decrease in the response. The second phase (100 nM-3 μM) was marked by increases in the twitch amplitude, caused desensitization of TRPV1, and the higher concentrations (10 μM-1mM) abolished the twitch response by non-specific mechanisms. Exogenous CGRP decreased twitch responses and its receptor antagonist blocked these responses in a competitive manner. The addition of CGRP receptor antagonists caused a potentiation of the twitch response and this potentiation was blocked by pretreatment with capsaicin and enhanced by incubation with exogenous CGRP. During a consecutive cumulative concentration responses curve (CRC) with capsaicin the first phase of CRC disappeared and this was partially restored when MVD were preincubated with CGRP, suggesting the release of exogenous CGRP by nerves.

Conclusion: This study indicates that exogenous CGRP can be taken up in MVD and this CGRP can be released in a manner similar to that of endogenous CGRP. CGRP uptake will add another dimension in understanding the homeostasis of this neuropeptide.

PS1-88
Differences in cgrp release profile between male and female rats
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Background and purpose: Migraine is 2-3 times more prevalent in women and the prevalence varies according to different reproductive milestones in females’ life. Therefore female sex hormones are implicated, but the exact mechanism behind this observed sexual dimorphism in migraine prevalence is not understood. In the present study we explored whether there are differences in basal and stimulated release of calcitonin gene-related peptide (CGRP) from dura mater between males and females, and effect of estrogen on the CGRP release. CGRP is a vasodilatory peptide which is extensively distributed in afferent nerves in the dural vasculature, and is the key neuropeptide implicated in migraine pathogenesis.

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Experimental approach: Male SD rats were either sham operated or orchidectomised, and subsequently treated with placebo, 17beta-estradiol or testosterone pellets for 21 days. Age matched female SD rats were also studied. After 21 days rats were sacrificed and hemi-sected skull model was employed to study the basal and KCl (60 mM) stimulated CGRP release.

Key results: The basal as well as KCl-induced CGRP release was significantly higher in female as compared to male rats. In orchidectomised rats 17beta-estradiol treatment led to an increased basal CGRP release whereas testosterone treatment reduced the CGRP release similar to the levels observed in sham operated male rats.

Conclusion and implications: This study shows that there is an increased CGRP release from dura mater of female rats and 17beta-estradiol positively influences the CGRP release, and this may be a key mechanism responsible for the sexual dimorphism in migraine prevalence.

PS1-89
Calcitonin gene-related peptide does not cause migraine attacks in patients with familial hemiplegic migraine
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Background: Calcitonin gene-related peptide (CGRP) is a key molecule in migraine pathogenesis. Intravenous CGRP triggers migraine-like attacks in patients with migraine with aura (MA) and without aura (MO). In contrast, patients with familial hemiplegic migraine (FHM) with known mutations did not report more migraine-like attacks compared to controls. Whether CGRP triggers migraine-like attacks in FHM patients without known mutations is unknown.

Objective: We examined the migraine inducing effect of CGRP in FHM patients without known mutations and healthy controls.

Methods and design: 11 FHM patients without known mutations and 11 controls received an intravenous infusion of 1.5 µg/min CGRP over 20 min. The study design was a balanced and controlled provocation study. Headache and other migraine symptoms were scored for one hour and self recorded hourly thereafter until 13 h post-infusion.

Results: We found no difference in the incidence of migraine-like attacks between the two groups, with 9 % (1 of 11) of patients and 0% (0 of 10) of controls reporting migraine-like headache (P = 1.00). CGRP infusion did not induce aura symptoms in any of the participants. There was no difference in the incidence of CGRP-induced delayed headaches between the groups (P = 0.18).

Conclusion: In contrast to patients suffering from MA and MO, CGRP infusion did not induce more migraine-like attacks in FHM patients without known mutations compared to controls. It seems that the majority of FHM patients with and without known mutation display no sensitivity to CGRP signalling compared to common types of migraine.

PS1-90
Sodium mri in a rat migraine model and a neuron simulation study support a role for sodium in migraine
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Introduction: Increased lumbar cerebrospinal fluid (CSF) sodium has been reported during migraine. We used ultrahigh field MRI to investigate cranial sodium in a rat migraine model, and simulated the effects of extracellular sodium on neuronal excitability.

Methods: Behavioral changes in the nitroglycerin (NTG) rat migraine model were determined from von Frey hair withdrawal response and photography. Central sensitization was measured by counting cFos-immunoreactive cells in the trigeminal nucleus caudalis (TNC). Sodium was quantified in vivo by ultra-high field sodium MRI at 21 Tesla. Effects of extracellular sodium on neuronal excitability was modeled using NEURON software.

Results: NTG decreased von Frey withdrawal threshold (p = 0.0003), decreased eyelid vertical height:width ratio (p < 0.0001), increased TNC cFos stain (p < 0.0001), and increased sodium between 7.5 and 17% in brain, intracranial CSF, and vitreous humor (p < 0.05). Simulated neurons exposed to higher sodium have more frequent and earlier spontaneous action potentials, and corresponding earlier sodium and potassium currents.

Conclusions: In the rat migraine model, sodium rises to levels that increase neuronal excitability. We propose that rising sodium in CSF surrounding trigeminal nociceptors...
increases their excitability and causes pain and that rising sodium in vitreous humor increases retinal neuronal excitability and causes photosensitivity.

**PS1-91**

**Enhancement of photic responses in upper cervical spinal cord neurons following dura inflammation in rats**

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It has been reported that upper cervical spinal cord (C1-C2) nociceptive neurons respond to strong photic stimulation as well as the intracranial dural stimulation. This may thought to be the mechanism underlying photophobia. However, the detail mechanism underlying photophobia is still unknown. In this study, to clarify the mechanism of photophobia, the change in the excitability of dura/light-sensitive nociceptive (DL) neurons was analyzed in rats with mustard oil administration to the dura (MO rats).

For this purpose, eye blink reflex, phosphorylated ERK-like immunoreactive (pERK-LI) cells in C1-C2 and the excitability of DL neurons to photic stimulation in MO rats were analyzed.

The number of eye blinks following strong photic stimulation was significantly larger in MO rats compared to vehicle rats. Strong but not weak photic stimulation also caused ERK phosphorylation in C1-C2 neurons in vehicle rats. On the other hand, a large number of pERK-LI cells was expressed in C1-C2 following weak photic stimulation in MO rats. Twelve DL wide dynamic range (WDR) neurons were found in the ventral area of C1-C2 spinal dorsal horn. The baseline activity and photic responses of the DL WDR neurons were significantly enhanced following MO administration. The receptive field size was also significantly expanded after MO.

The present findings suggest that an enhancement of DL neuronal activity may have important roles underlying photophobia in migraine.

**PS1-92**

**Cb1 receptors are involved in the olvanil-induced inhibition of nociceptive trigeminal activation**

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Transient receptor potential vanilloid receptor subtype 1 (TRPV1) are located on trigeminal fibers innervating the dura mater and colocalize with calcitonin gene-related peptide (CGRP). Olvanil is a weak TRPV1 agonist that desensitizes neuronal fibers but does not induce a significant CGRP release, and lacks pungency. Recently, we demonstrated olvanil inhibits neuronal transmission in the trigeminovascular system. The aim of the present study was to investigate whether this effect is exclusively mediated by TRPV1 receptors, or if it may involve CBI receptors.

In male Sprague-Dawley rats under general propofol anesthesia the middle meningeal artery (MMA) was stimulated through a cranial window and electrophysiological activity of second order neurons was recorded in the trigeminocervical complex (TCC). Experimental groups received intravenously either olvanil (5 mgkg⁻¹) alone or olvanil preceded by the TRPV1 receptor antagonist A993610 (8 mgkg⁻¹), or the CB1 receptor antagonist AM251 (3 mgkg⁻¹) 5 minutes prior to the olvanil administration. The effects on trigeminovascular activity were recorded over 45 minutes after olvanil administration.

As demonstrated in our previous study olvanil significantly inhibited stimulus-evoked cell firing in the TCC (p < 0.05) thereby acting like an inverse agonist. However, the inhibitory action of olvanil on the stimulus-evoked activity of trigeminovascular neurons could be attenuated by the intravenous administration of either the TRPV1 receptor antagonist A993610 or the CB1 receptor antagonist AM251. These results demonstrate for the first time in an in vivo model relevant for migraine, that the effect of the TRPV1 agonist olvanil involves in some part CBI receptors.

**PS1-93**

**The induced release of cgrp by peripheral or central administration of inflammatory soup does not depend on nitric oxide**

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Calcitonin gene-related peptide (CGRP) is released during activation of the trigeminal nerve system. Clinical and experimental studies have demonstrated that CGRP is a crucial neuropeptide in the pathophysiology of migraine as it modulates neuronal activity in the trigeminocervical complex (TCC) and the blockage of its receptor is effective in the acute treatment of migraine.

We have recently demonstrated, that the intracisternal administration of Inflammatory Soup (IS) induces release of CGRP into CSF and the peripheral circulation from central and peripheral trigeminal neurons. We hypothesize, that peripheral administration of IS leads to a CGRP release into jugular vein blood comparable to what we have seen after central IS administration. Moreover, we hypothesize that IS-induced CGRP release is not mediated by nitric oxide (NO).

In male Sprague-Dawley rats IS was administered into the cisterna magna or into the femoral vein and blood samples were collected from the jugular vein for analysis of CGRP concentration. In order to test a possible mediating effect of NO, a separate group of animals received a pretreatment with the unspecific NO-synthase inhibitor L-NAME before administration of IS.

Intracisternal IS-administration led to a significant increase of CGRP into the extracerebral circulation (p < 0.001). L-NAME did not inhibit IS-induced CGRP release. Peripheral administration of IS (200 μl) did also cause CGRP release after 2 and 15 minutes (p < 0.001) whereas IS vehicle was without effect. We conclude that central and peripheral IS administration lead to CGRP release which is not NO dependent.

PSI-94

Chronic cerebral hyoperfusion results in selective disruption of white matter; an in vivo MRI study with implications for post spreading depression hyoperfusion


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Background and aims: Aura and cortical spreading depression (CSD) result in blood flow alterations and cerebral hypoperfusion. Migraine with aura predisposes individuals to an increased risk of white matter (WM) lesions which correlate with attack frequency. As hypoperfusion is a risk factor for WM disruption in ageing we sought to explore the outcome of mild chronic cerebral hypoperfusion (CCH) on WM integrity in a novel mouse model.

Methods: Mice (25-30g) were anaesthetised and CCH induced via carotid artery stenosis using 0.18mm-i.d. microcoils. Following 1 month CCH (n=14) or sham procedure (n=7), diffusion tensor and magnetisation transfer imaging data were collected using a Varian-7T preclinical scanner. Fractional anisotropy (FA) and magnetisation transfer-ratio (MTR) maps were generated and appropriate WM regions-of-interest were selected from T2-weighted maps. Following MRI, brains were processed for evaluation of white and gray matter pathology.

Results: Significant reductions in FA were observed in the corpus callosum and internal capsule, and significantly decreased MTR was observed in the corpus callosum, fimbria, internal capsule and optic tract following hypoperfusion. Hypoperfused mice demonstrated diffuse axonal and myelin pathology which was essentially absent in sham mice. Both FA and MTR correlated with immunohistochemical markers of myelin integrity/degradation and not axonal pathology.

Conclusions: One month of mild CCH results in a selective disruption of WM as measured in vivo using MRI. Given the link between migraine aura, CADASIL, hypoperfusion and WM lesions, prevention of cerebral blood flow alterations such as those seen in aura and ageing may be crucial to limit adverse outcomes.

PSI-95

Nxn-188 during the aura phase of migraine with aura: a randomized, double-blind, placebo-controlled cross-over study

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Background and aims: NXN-188 is an oral therapeutic which has previously shown efficacy in the acute treatment of migraine. NXN-188 inhibits neuronal nitric oxide synthase (nNOS) and is also a 5HT-1B/1D receptor agonist. The NOS inhibiting action is probably important because NO is involved in the pathogenesis of migraine pain and is formed after cortical spreading depression.
Therefore NXN-188 could prevent the development of the headache phase in migraine with aura if taken during the aura. This would provide an advantage over the triptans which have been shown to be ineffective if given during migraine aura. The aim of this study was to evaluate the efficacy and safety of NXN-188 600 mg in the acute treatment of migraine when dosed during the aura.

Methods: A single-center, randomized, double-blind, placebo-controlled, two-way crossover trial. The study medication was taken during the aura and the patients kept a study diary for 48 h post-dose. Patient inclusions (N = 49) ended on November 1st and at the moment 11 patients are still in the study. The study will end in March 2011 after which data will be analyzed. Full data will be presented at the IHS meeting.

Results: The results are currently pending as the data are still blinded.

Conclusion: This is a study of a new class of drug for the treatment of acute migraine. Its dual-action may abort the headache phase of migraine with aura.

A positive outcome would support a role of NO in the pain of migraine with aura.

PS1-96
Isolating the effect of headache triggers using propensity scores

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Background: Headache patients are often encouraged to keep a diary to identify their headache triggers. Yet, it is difficult to isolate the unique effect of a single trigger when it is observed in a sea of confounding influences, or other triggers. This study demonstrates the use of propensity methodology to isolate the effect of a trigger while efficiently controlling for a large number of other triggers.

Methods: Propensity score methodology (Rosenbaum & Rubin, 1983) is a popular method for adjusting observational data for potential confounders, but has not been used in headache trigger studies. The present study describes a mathematical simulation where 200 episodic headache sufferers (<15 days/month) were simulated as having collected a 3-month daily diary of 20 potential headache triggers. The headache triggers contained various levels of associations with each other (r = 0 to 0.75) and varying potency for inducing a headache (OR = 1.0 to 6.0). In other models, associations between triggers acted only through mediators, such that after adjusting for the mediating influence the observed association should be eliminated.

Results: Using propensity scores, the confounding effects of confounding influences under a variety of conditions could be adjusted, even in the presence of differing levels of autocorrelation among the confounders. Estimation issues were encountered with very low headache frequency (<2 headache days).

Conclusions: Propensity score methodology has substantial utility for isolating headache triggers in research studies and individual patient diaries. Strengths and weakness of the approach are discussed among derived sample size estimates.

PS1-97
Double blind study of topical salicylate with photoprotective mask as treatment for migraine and/or tension headaches

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Objective: A placebo-controlled double-blind study was performed to determine the efficacy of a topical anticephalgic premedicated mask in the treatment of migraine and/or tension headaches.

Design/methods: The patients were given masks and numbered bottles of topical medication containing topical salicylates or placebo. They were instructed to apply the medication to their frontalis region in the event they should suffer a headache, put on the photoprotective mask. Furthermore, they were instructed to take oral medications, if required, for relief of the headache.

Results: Seven out of 20 of the patients who received the placebo stated the medication and mask helped and gave it an average rating of 4.31 on a 0-10 scale. Twenty-eight out of 34 of the patients receiving the active medication stated it was effective, rating it 7.42 on the 0-10 scale. Furthermore, the majority of the patients receiving the
active medication stated the duration of their headaches was significantly reduced as was their need for analgesic and/or narcotic medications for relief of the headaches.

**Conclusion:** This study demonstrates a significant difference between the placebo and the true medication in association with the photoprotective mask in treating migraine and/or chronic muscle tension headaches.

**PSI-98**

**Treatment strategies in chronic daily headache with drug abuse**

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**Introduction:** It is well known that chronic use analgesic induces headaches. Analgesic abuse is a common problem with migraine patients. It is characterized by a reported increase in the frequency and intensity of pain attack, inducing transformation of a periodic headache into a CDH. Treatment can be in an outpatient setting, but often patients require hospitalization to help to discontinue drug abuse.

**Patients and method:** The results obtained from two group of CDH patients with drug abuse evolving from atypical migraine. Patients were hospitalized for drug withdrawal and then followed regularly in order to determine clinical improvement after withdrawal. The first group were studied from September 2009-February 2011 (Group A 15 subjects) was treated using pharmacological prophylactic therapy; the second group (Group B 7 subjects) was treated using pharmacological and psychotherapy-assisted training behavior. A statistically significant improvement in both groups was found, with reduction in pain total index, days of headache/month and decrease on analgesic consumption. This improvement was maintained at 1-year follow-up.

**Discussion:** At present it is not possible to identify differences between the two treatment groups, pharmacological versus pharmacological and behavioral therapy: psychotherapy-assisted training does not seem to favor a better resolution of the drug abuse problem. Adequate prevention may be obtained by educating the patient and family regarding the risk of analgesic overuse; by adequate prescription and information of the side-effects and by a close clinical monitoring of changes in headache pattern and drugs used.

**PSI-99**

**Development of a model to study trigeminal cgrp release in human subjects**

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Levels of calcitonin gene-related peptide (CGRP) are increased during migraine. TRPV1 receptors on trigeminal sensory nerve endings may mediate CGRP release. Thus, increased CGRP release during migraine may be either due to increased sensitivity of the TRPV1 receptor, or due to an increased amount of CGRP in perivascular nerve terminals. Capsaicin, the pungent ingredient of chili peppers, stimulates TRPV1 receptors and causes CGRP-dependent vasodilatation, thereby increasing blood flow. We developed a model to study trigeminal CGRP release in humans. We compared the vasodilator effects of application and iontophoresis of capsaicin on the forearm skin. Subsequently, we characterized the effects of iontophoresis on the forehead, which is innervated by the trigeminal nerve. Subjects were studied with a Laser Doppler Imager twice. On the forearm, two electrodes with a reservoir were filled with a 20 mM capsaicin solution. Iontophoresis was performed on one reservoir and the increase in blood flow was measured. Experiments were repeated on the forehead, including detailed characterization of the iontophoresis effects. On the forehead, capsaicin iontophoresis (Emax: 316 ± 14 u.a.) induced more vasodilatation than application of capsaicin (Emax: 282 ± 18 u.a., P < 0.01). Emax was reached faster (18 ± 1 min vs. 32 ± 2 min, P < 0.001) and was well reproducible. On the forehead, we determined the contribution of iontophoresis (Emax after iontophoresis of saline: 262 ± 71) to the effects of capsaicin iontophoresis (Emax: 424 ± 110). In conclusion, knowledge about the contribution of iontophoresis effects allows us to discriminate between effects due to capsaicin (via TRPV1 receptors) and electrical stimulation of the trigeminal afferents. This model is well suitable to study trigeminal CGRP release in humans.

**PSI-100**

**Brachial-ankle pulse wave velocity and ankle-brachial index in midlife migraineurs without cardiovascular disease risk factors**

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Background: Migraine is associated with an increased risk for ischemic stroke and cardiovascular disease (CVD).

Purpose: We aimed to evaluate arterial pulse wave velocity (PWV) and ankle-brachial index (ABI) in Japanese middle-aged migraineurs.

Methods: Brachial-ankle PWV (baPWV) and ABI, using an oscillometric technique (form PWV/ABI, BP-203RPE II), were measured in 111 migraineurs (81 women and 30 men) and 110 controls matched by age, sex and blood pressure. All participants had no CVD risk factors and prior history of CVD. Cut-off value of normal ABI was 0.9.

Results: Twenty-two subjects had migraine with aura and 89 had migraine without aura. Mean age (SD) of migraineurs was 44.4 (9.3) years [44.7 (9.0) in women and 43.0 (10.1) in men]. Migraine duration (SD) was 18.0 (10.8) years [18.7 (11.3) in women and 17.0 (10.4) in men]. Attack frequency was 71 subjects in ≥ 1 time/month and 40 subjects in < 1 time/month. Mean baPWV (SD) of migraineurs was 1247 (189) cm/sec in women and 1356 (126) in men. That of controls was 1138 (136) in women and 1250 (121) in men. baPWV was significantly increased in female and male migraineurs (p < 0.05). Mean ABI (SD) was 1.05 (0.06) in migraineurs and 1.06 (0.07) in controls. ABI did not differ between migraineurs and controls. Only one migraineur without aura had abnormal ABI. Clinical variables of migraineurs were not associated with data of baPWV and ABI.

Conclusions: Our data indicated that increased baPWV could reflect arterial dysfunction in midlife migraineurs without CVD risk profile.

PS1-101

Effect of cortical spreading depression on the phosphorylation of erk in the trigeminal ganglion of rat


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Introduction: In migraine pathophysiology, cortical spreading depression (CSD) and activation of the trigemino-vascular system are known to contribute to aura and headache, respectively. However, the relation between CSD and activation of the trigeminal nerve is still obscure. Phosphorylation of extracellular signal-regulated kinase (ERK) in sensory neurons by noxious stimulation is known to contribute to pain hypersensitivity, and we have already reported the occurrence of phosphorylation of ERK in the trigeminal ganglion (TG) after stimulation of dural TRPV1 receptor. In this study we examined the effect of CSD on the phosphorylation of ERK in the TG.

Methods: Twelve SD male rats were used. After 1M KCl application into cranial window installed in the bilateral temporo-parietal region, DC potential was recorded with electrodes fixed on the bilateral rostral edge of the cranial window, and transient depression of DC potentials were detected as CSD (n = 6). For control, saline was applied into the cranial window (n = 6). Thirty minutes later, bilateral trigeminal ganglia were dissected for western blot analysis to observe the expression of pERK and total-ERK. The ratios of the intensity were calculated.

Results: During 30 minutes after KCl application, CSD was observed at 6.3 ± 2.0 times, while there were no CSD after saline administration. In CSD evoked group, the ratios of pERK/total-ERK displayed significantly higher levels compared with control (1.82 ± 0.48 for ERK1 (n = 6) and 2.97 ± 0.76 for ERK2 (n = 6)).

Conclusion: These findings raised the possibility that CSD may activate the trigemino-vascular system and become the trigger of migraine headache.

PS1-102

Estrogen reduces cerebrovascular tone through endothelial-dependent and endothelial-independent mechanisms

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Background and aim: Estrogen has well known vaso-protective effects and fluctuations in estrogen levels are suggested to be involved in menstrual migraine. It was previously demonstrated that in cerebral arteries, estrogen affects contractility by enhancing the release of the endothelial vasodilators nitric oxide (NO) and prostacyclin. These effects involve both genomic and non-genomic mechanisms, activation of the estrogen receptor (ER) alpha increases expression of endothelial nitric oxide synthase (NOS) mRNA and protein as well as phosphorylation of NOS by Akt.

Methods: We studied the effect of estrogen and agonists selective for ERalpha and ERbeta on isolated basilar arteries from female mice. Arterial segments were mounted in myographs containing Krebs buffer solution.
Results: Isolated, precontracted segments of basilar artery relaxed upon exposure to either estrogen (EC50 = 1 μM) or the ERα agonist PPT (EC50 = 0.7 μM); these effects were inhibited by the ER antagonist fulvestrant. In contrast, DPN, an ERβ agonist, was relatively ineffective. Surprisingly, the effects of estrogen and PPT were not blocked by inhibitors of NO synthase or cyclooxygenase, nor did they require the presence of functional endothelium.

Conclusion: The study shows a mechanism by which estrogen acutely alters cerebrovascular tone independent of endothelial mechanisms. We suggest that estrogen not only increases NOS and prostacyclin expression in cerebrovascular endothelial cells but, also causes a direct relaxation via activation of ERα receptors located in the smooth muscle cells of cerebral arteries.

PSI-103
Comparison of interictal platelet activation in episodic migraine aura with and without patent foramen ovale

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Objective: Determine if interictal platelet activation is more common in migraine aura (MA) when associated with patent foramen ovale (PFO) and right-to-left shunt (R-L-S).

Background: Platelet activation may occur as blood is shunted across a patent foramen ovale (PFO), producing microaggregates that trigger cortical spreading depression and MA.

Methods: Subjects aged 18-55 y with MA (ICHD-2) and 4-14 migraine d/mo were evaluated for PFO using transcranial Doppler; subjects were grouped according to grade (R-L-S group, Grade ≥IV/V following Valsalva; control group, Grade ≤IV at rest and Valsalva). Major exclusion criteria included stroke; antipatelet, antiplatelet, or anticoagulant use; severe anxiety/depression. Cognitive function was assessed using 8 performance-based neuropsychological tests in 3 domains: learning/memory; cognitive efficiency/attention; processing speed. Tests were administered ≥24 h after sedative/alcohol ingestion and migraine resolution.

Results: 17 subjects (34±11 y, 82% female) in the R-L-S group and 10 subjects (35±9 y, 85% female) in the control group comprised the sample. Migraine burden (migraine, 7±3 d/mo vs. 8±3 d/mo, p=0.6; MIDAS, 40±46 vs. 38±33, p=0.9; HIT-6, 62±8 vs. 66±5, p=0.1) was not significantly different between R-L-S and control groups, respectively. Platelet activation was not different between groups (all ng/mL: P-selectin 39.7±17.1 vs. 46.0±26.0, p=0.5; sCD40L 1.2±1.4 vs. 1.3±1.8, p=0.8; TXB2 99.7±91.5 vs. 181.7±177.5; p=0.1).

Conclusions: In this interim analysis, platelet activation was not increased when PFO and large R-L-S coexisted with MA, suggesting that platelets are not activated within the PFO tunnel. Future research is needed to determine if a causal mechanism exists between MA and PFO.

PSI-104
Effect of patent foramen ovale (pfo) with large right-to-left shunt (r-l-s) on interictal cognitive function in episodic migraine aura (ma)
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Objective: Compare interictal cognitive function in MA with and without large R-L-S.

Background: Migraine attacks are theorized to result in mild cognitive impairment due to repeated vascular insult. Coexistence of PFO permits shunting of microaggregates to the cerebral vasculature, producing recurrent transient ischemia and increasing risk of cognitive impairment.

Methods: Subjects aged 18-55 y, with ≥2 y history of MA (ICHD-2) and 4 -14 migraine d/mo were evaluated for PFO using transcranial Doppler; subjects were grouped according to grade (R-L-S group, Grade ≥IV/V following Valsalva; control group, Grade ≤IV at rest and following Valsalva). Exclusion criteria included stroke; MS; TBI; topiramate, antiplatelet, or anticoagulant use; severe anxiety/depression. Cognitive function was assessed using 8 performance-based neuropsychological tests in 3 domains: learning/memory; cognitive efficiency/attention; processing speed. Tests were administered ≥24 h after sedative/alcohol ingestion and migraine resolution.

Results: 19 subjects with R-L-S (34±10 y, 84% female) and 12 controls (36±9 y, 83% female) comprised the
sample. Subjects had high migraine burden (migraine d/mo 7.8±3.1 vs. 7.8±2.9, p=0.0; MIDAS 43±45 vs. 35±30, p=0.6; HIT-6, 62±8 vs. 65±3, p=0.2). College education (68% vs. 50%, p=0.6) and full-time employment status (58% vs. 58%, p=0.8) were similar between groups. Mean standardized scores in all domains were ±1 SD of average (93-110) with no significant group differences (p>.01). HIT-6 scores were inversely correlated with auditory learning/memory (r -.35 to -.49, p<.05).

Conclusions: In MA with high burden, presence of PFO with large R-L-S had no significant effect on cognitive function. High migraine burden may affect interictal auditory learning/memory.

PS1-105
Comparison of sleep apnea (sa) in episodic migraine aura (ma) with and without patent foramen ovale (pfo) with large right-to-left shunt (r-l-s)

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Objective: Compare prevalence of SA between MA with and without PFO with large R-L-S.

Background: PFO occurs frequently in MA and SA; however, a direct causal link is not established. The prevalence of SA in MA with PFO has not been evaluated.

Methods: Subjects with MA, aged 18-55 y, and monthly migraine frequency (MMF) of 4-14 d/mo were evaluated for PFO using transcranial Doppler; subjects were grouped according to grade (R-L-S, ≥IV/V following Valsalva; control, ≤I/V at rest and following Valsalva). Exclusion criteria included stroke; TBI; MOH; prior CPAP use. Procedures were initiated >24 h after alcohol/sedative use and migraine resolution. Subjects underwent a home sleep study using a portable monitor with oximetry; ≥5 h of recorded data was analyzed for apnea-hypopnea index (AHI) and oxygen desaturation index (ODI). AHI >10 events/h constituted SA.

Results: 15 R-L-S (34 y±11, 12 [80%] female) and 9 control subjects (33 y±9, 8 [89%] female) were enrolled. Migraine burden was high (MMF 7±3 vs 8±3, p=.3; MIDAS 42±49 vs 42±33, p=.68; HIT-6, 61±9 vs 67±5, p=.17). Body mass index (BMI; 25.8±4.2 vs 29.7±10.2, p=.3) and neck circumference (35±3 vs 35±9, p=.9) were similar. AHI and ODI were higher in controls (AHI 1.7±1.8/h vs 3.8±2.4/h, p=.01; ODI 1.4±2.1/h vs 2.7±2.6/ h, p=.16). 1 R-L-S and 3 controls had AHI 5-10/h. ODI but not AHI was correlated with age, BMI, and waist circumference (r=-.41-.49, p<.05).

Conclusions: Interim analysis suggests that SA is not more prevalent in MA with PFO and large R-L-S.

PS1-106
Basilar artery vasomotor reactivity in episodic migraine aura with patent foramen ovale (pfo) and large right-to-left shunt

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Objective: Compare basilar artery (BA) vasomotor reactivity (VMR) in migraine aura (MA) with and without PFO and large right-to-left shunt (R-L-S).

Background: Stroke in MA occurs more frequently in the posterior region, suggesting BA involvement. It is plausible that PFO with R-L-S, found in 50% of MA, permits microemboli to bypass pulmonary filtration and may result in endothelial dysfunction and altered VMR.

Methods: Subjects aged 18-55 y with MA (ICHD-2) and 4-14 migraine d/mo were evaluated for PFO using transcranial Doppler (TCD); subjects were grouped according to grade (R-L-S, ≥IV/V following Valsalva; control, ≤I/V at rest and Valsalva). Exclusion criteria included stroke; MS; TBI; fetal origins; carotid stenosis; antiplatelet, anticoagulant use. Procedures were initiated ≥24 h following sedative or anti-hypertensive drug use and migraine resolution. BA velocities were measured at baseline; following inhalation of 6% CO2:94% O2 for 3 m; following hyperventilation to ETCO2 < 25 mmHg.

Results: 21 R-L-S (aged 34±10 y, 86% female) and 10 control subjects (aged 35±9 y, 90% female) comprised the sample. Migraine burden was similar between groups (frequency 8±3 vs. 8±3 d/mo, p=.08; MIDAS 40±42 vs. 38±33, p=.9; HIT-6 62±8 vs. 66±5, p=.02). Baseline velocities (49±11 vs 42±14 cm/s, p=.2) and VMR (96±29 vs 87±21, p=.4; % velocity change/mmHg CO2, 3.9±1.3 vs. 3.6±8, p=.4) were similar between groups.

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VMR was not correlated with TCD embolic tracks at rest (r = -.1, p = .7).

Conclusions: Results indicate that BA VMR as a measure of endothelial dysfunction does not differ between MA with and without large R-L-S.

PSI-107
A thorough qt study comparing supratherapeutic dose of orally inhaled dhe, moxifloxacin, and placebo on the qt interval in healthy volunteers
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Objective: To assess effect of LEVADEX™ (MAP0004, orally inhaled DHE) on QT interval. Three treatments, a supratherapeutic dose of MAP0004 (3.0 mg), 400 mg moxifloxacin and placebo were assessed using Fridericia and Individualized correction formulas.

Background: MAP0004 is an orally inhaled formulation of dihydroergotamine mesylate. Although DHE has been used clinically for many years and has not been associated with cardiac arrhythmias, no thorough QT study has been performed on DHE by any route of administration. Prolongation of the cardiac QT interval is associated with syncope and/or sudden cardiac death due to arrhythmia and is a known side effect in more than 50 marketed drugs.

Methods: Phase I, double-blind, placebo-controlled, three-period crossover study. Triplicate electrocardiograms were performed at predose baseline and continuously over 24 hours post-dose. Fifty-four healthy adults completed the trial and had measurable plasma levels of DHE after the supratherapeutic MAP0004 dosing.

Results: The largest mean difference in the corrected QTcl between MAP0004 and placebo was 0.08 msec and the largest one-sided 95% upper confidence bound was 2.24 msec, both at 30 minutes after dosing. In contrast, moxifloxacin increased the mean QTcl between 9.57 and 11.28 msec relative to placebo, with a one-sided lower 95% confidence bound between 7.23 and 8.96 msec. Nausea was common following 3.0 mg MAP0004 dosing (27.8%), but did not appear to influence the QT interval.

Conclusions: A supratherapeutic dose of orally inhaled DHE, approximately three times the intended clinical MAP0004 dose, did not prolong QTc intervals.

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PSI-108
Substance use in and personality profiles in cluster headache
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Background and aims: Studies about an increased substance use in patients with cluster headache (CH) showed partly ambiguous results and did not focus on different subgroups of cluster headache in comparison to migraine patients and healthy controls. Furthermore, the influence of personality traits such as “reward-dependance” is unknown. Therefore, this study aimed to examine substance use and personality traits in these groups.

Methods: In a multicentre prospective study patients with chronic CH (n = 27), episodic CH in the active (n = 26) and outside the active period (n = 22), migraine patients (n = 24) and healthy controls (n = 31) were included. Epidemiological data, Fagerström nicotine dependence test (FTND), Alcohol Use Disorders Identification Test (AUDIT), a caffeine questionnaire and the Tridimensional Personality Questionnaire (TPQ) were collected.

Results: In CH patients, smoking was significantly more common with higher levels of dependence than in the other groups. While AUDIT scores did not differ, hazardous drinking was found significantly more often in CH patients (especially chronic patients). Likewise, caffeine consumption was highest in CH patients. Personality traits (FTQ scores) did not differ.

Discussion: CH increases the risk of substance use (especially nicotine and caffeine). However, a certain subgroup of patients could be protected by the attack inducing potential of alcohol. Interestingly, personality traits did not differ between patients with CH, migraine and controls. Thus, other mechanisms specific to cluster headache could be responsible such as changes in the orexigenic system which has been suggested to play a potential role in both nociception in cluster headache and substance use.
Efficacy of mirtazapine for treatment of medication-overuse headache (moh) a in 3 cases of moh

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Introduction: We experienced successful treatment by Mirtazapine for 3 cases of MOH.

Case1: 51 years old, female.
Case2: 50 years old, male.
Case3: 48 years old, female.

A migraine headache started in the teens in all case. These headaches gradually became chronic by abuse such as OTC drugs. Then treatment was started in the outpatients office of our Neurology. Clinical condition of transformed migraine was presented in all cases. It was denied with depression, anxiety disorders based on the criteria of DSM-IV. However subjective insomnia, anxiety and hypochondria were seen.

Therefore Hamilton Depression Scale (HAM-D) was an average of 12 points and comparative high score. All cases were diagnosed as "suspecting MOH (8.2.8 of ICHD-II). According to it, the medication thought to be as the stopped and mirtazapine 15mg/day was chosen as preventive drug. From start of therapy about 1 week later, the degree of a headache was ameliorated. These psychiatric symptom such as insomnia and anxiety in HAM-D decreased. No recurrence of MOH was seen more than one year in all cases.

Discussion: Mirtazapine accelerates direct increases of secretion in both serotonin and noradrenaline via different mode of action such as SSRI, SNRI. Thereby, improvement of serotonin depletion and activating decending pain modulatory system may cause improvement of these MOH cases. These case reports suggest that mirtazapine may also be one of the useful option in the treatment of MOH.

Efficacy of continuous positive airway pressure therapy for migraines in sleep apnoea syndrome

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Background and aims: The frequency of obstructive sleep apnea syndrome (OSAS) in migraine is comparable to the general population. Hypoxia might be a trigger for migraine. Continuous positive airway pressure (CPAP) therapy improves morning headache in OSAS and seems to be effective in cluster headache. There is little known on the effect of CPAP therapy on migraine in OSAS patients.

Methods: We assessed frequency and characteristics of migraine patients in OSAS and the effects of CPAP therapy on migraine. Patients were assessed by medical history, clinical examination, sleep and headache questionnaires, video-polysomnography (PSG) and routine blood tests at baseline before and at follow-up one year after treatment with CPAP. Sleep apnea was defined as apnea-hypopnea-index (AHI) > 15. All patients were free of migraine prophylaxis or other CNS medication.

Results: Twelve (9.9%, eight men) out of 121 consecutive OSAS patients fulfilled diagnostic criteria for migraine. The mean attack frequency was 5.9 (±7.4 SD) per month before and 0.2 (±0.3 SD) after one-year CPAP treatment (p < 0.05). Mean acute anti-migraine medication intake was 6.8 (±8.1) units per month and 0.1 (±0.1), respectively (p < 0.05). Slow wave sleep (13% vs. 23% total sleep time (TST), p = 0.001) and oxygenation time (< 90% S O2: 23.5% vs. 2.1% TST, p = 0.03) improved. No significant differences between migraineurs and non-migraineurs were found.

Conclusion: Continuous positive airway pressure (CPAP) given for one year to patients with migraine and obstructive sleep apnea syndrome significantly decreases the frequency of their migraine headaches.

Topiramate and cerebral vasomotor reactivity in migraine

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Background and objective: Migraine is a common neurological disorder that affects daily activities and impair quality of life. Topiramate (TPM) is an antiepileptic with broad-spectrum and has multiple mechanisms of action. It is a prophylaxis choise of migraine. In this study, our aim is to compare cerebral vasomotor reactivity(VMR) in patients with migraine before and after TPM
prophylaxis, and also compare this group with control (having no migraine) group.

Methods and materials: 20 migraine patient underwent cerebral vasomotor reactivity measurement using transcranial doppler (TCD) imaging of the middle cerebral artery (MCA) before and after TPM treatment. Their visual analog scale (VAS), attack frequency and number of attacks per month were noted before and after treatment. And also 20 control group patient underwent VMR measurement.

Results: Migraine group’s VMRs are greater than the control group, but after TPM treatment their VMRs became similar. A statistically significant decrease in VMR and VAS scores, attack frequencies and number of attacks per month were seen in the migraine group after treatment.

Conclusion: Cerebral vasomotor reactivity (VMR), is the capacity to meet the cerebral circulation and blood flow velocity (decrease and increase) based on changes in cerebral metabolic changes. VMR is important for the othonomic and hemodynamic functions of cerebrum. And also it can be used to detect the efficacy of migraine prophylaxis. Our VMR results and VAS scores showed that TPM is an effective drug for prevention of migraine and reducing the severity of attacks.

PSI-112
The assessment of serum mmp-9, timp-1 levels and mmp-9/timp-1 ratio in migraine patients with and without aura during the headache and the painless episodes
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Matrix Metalloproteinases (MMP) are considered to have a role in the pathogenesis of migraine. In this study the serum levels of MMP-9 and the endogenous tissue inhibitor TIMP-1 during both the headache and painless episodes in migraine with and without aura were planned to be compared with that of a healthy control group. 50 migraine (25 with aura and 25 without aura) patients were participated. The control group consisted of 25 eligible volunteers. The sampling procedure was done once for the healthy control group and twice for the migraine group where the first samples were taken during the headache and second ones were taken in the painless episode. The serum TIMP-1 level of all migraine patients were found to be significantly lower than the control group in both headache episode and the painless episode samples (p < 0.01). The MMP-9/TIMP-1 ratio of all migraine patients were found to be significantly higher than the control group in both headache episode and the painless episode samples (p < 0.01). In this study an increase in net MMP-9 activity has been observed which can be considered as an indicator of the role of this enzymes disorder on neuroinflammation and the cortical spreading depression. On the other hand, the low level of TIMPs even in the painless episode, has revealed the fact that the proteolytic protection of migraine patients was considerably degraded and there might be a genetical difference compared with the individuals without migraine. With the help of extensive studies on this subject, the MMP-9 inhibitors and TIMP-1 agonists might become a new migraine treatment option in near future.

PSI-113
Biochemical marker of intensity of tension headache
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Objectives: Tension headache (TH) is the most frequent type of the idiopathic cephalalgies. Depression and serotonin metabolism disorders play a leading role in the pathogenesis of TH.

Methods and subjects: The complex algic, psychometric tests and investigation of blood serum and thrombocytes serotonin (S) concentration by the method of immunoenzyme assay were performed in 140 patients with TH.

Results: The intensity of episodic TH (44 man) was 56±4.32 mm according to 100-mm visual analogue scale in patients of the first group. All the patients of this group had high level of reactive anxiety (50.18±8.6, p=0.002), moderate level of depression and tendency to the decreasing of blood S concentration (205.72±21.62 ng/ml). The second group consisted of 96 patients with chronic TH. It was revealed significant decreasing of blood S concentration in serum (117.3±60.1 ng/ml, p=0.046 versus control group 256.8±24.38 ng/ml) and thrombocytes (280.9±63.25 ng/ml, p=0.031 versus control group 578.5±46.34 ng/ml). Straight correlation between duration and intensity of ache, levels of reactive and personal anxiety (46.81±8.8 and 54.2±9.64 accordingly), high depression level (23.6±4.52 points in according to Beck scale, p=0.001) and decreasing of blood S concentration was revealed in all patients of this group.
Conclusions: Concentration of blood serotonin depends on duration and intensity of ache, level of depression and anxiety. Therefore, blood serum serotonin can be used as biochemical marker of ache intensity in patients with tension headache.

PSI-114
Botulinum toxin A effectively treats severely disabling headache with dystonic features. An open-labelled prospective study
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In consecutive patients the role of dystonia and acceptance of botulinum toxin A (BTXA, Dysport®) treatment was examined in a tertiary headache clinic. Dystonic features in neck muscles may present in headache patients with muscle soreness and stiffness confined to neck muscles.

122 consecutive chronic headache patients (F=82; M=40; age=41.5±12.5), previously naïve to BTXA treatment with clinical signs of dystonic features were examined by a specialist neurologist. EMG guided measurement of activity(turns/second), average amplitude(mV) was done in neck muscles of interest if at minimum 200 turns/second was measured at least at 2 sites, the patients were informed of the possibility of BTXA treatment and if consent was obtained needle EMG guided BTXA was injected.

Headache duration >1 year; Median VASheadache=7.0 (25th;75th perc. 5.0;8.0); present VASheadache=5.0 (2.25;7.0); Worst VASheadache=10.0 (9.0;10.0). The HIT-6 scale (range 36-78) median score=65.00 (61.25;68.75). Maximum turns/second was higher in females (F=355.5±72.1; M=287.2±73.9; p<0.0002). In median 4.0 sites (3.0;4.0) a median of 150 units (100;150) BTXA was injected. Age; gender; diagnosis (G43.0; G43.1; G44.2; G44.3; G44.841; other) did not influence treatment response. During 4 months of observation 15.6% no effect; 22.1% temporary worsening; 7.4% slight improvement; 12.3% some improvement; 18.0% >2 months of 50% headache/neckpain reduction; 6.6% had >2 mths of headache free period. Complaints: heaviness of head (28%); initial neck pain (32%); others(<6%).

25% of severely affected dystonic headache patients gained 50%+ long-term pain relief, >50% wanted BTXA re-treatment. 1-year follow-up data will be presented. Double-blind RCTs are needed to confirm the promising results.

PSI-115
The effect of systemic leptin administration on cortical spreading depression model rats
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It is known that obesity is one of the risks of migraine chronication. Furthermore, it is known that the plasma level of leptin increases in obesity. In this time, we examined the effect of leptin on the rat cortical spreading depression (CSD) model to clarify the relation between leptin and migraine.

Methods: Five male Sprague Dawley rats weighing 380-450g were used. Leptine (0.1mg/kg/day) or saline was administered intraperitoneally once a day for 7 days (respectively n=5). After that, under anesthetizing condition by administering α-chloralose and urethane intraperitoneally, a tracheostomy was performed for controlled ventilation. To investigate physiological parameter and blood gas, right femoral artery was catheterized. A laser-Doppler probe was placed on the cerebral cortex through the left bone fenestration for measuring cerebral blood flow (CBF). The two other bone fenestrations were opened for measuring direct current (DC) potential of CSD, and for dropping KCl solution. After 1.0 mol KCl solution was dropped through the bone fenestration to induce CSD, we measured the CBF and DC potential.

Results: Leptine pre-treatment significantly decreased % change of CSD and DC potential, respectively, compared with vehicle rats. And leptine pre-treatment increased the number of CSD compared with vehicle rats significantly.

Conclusions: Percent change of CBF and DC potential was decreased and the number of CSD was increased by leptine. These results suggest that leptine modulates the pathological mechanisms of migraine.

PSI-116
Calcium signaling in neurons and glial cells of transgenic fhm1 mice
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**Aims:** As migraine is a common episodic excitability disorder the interplay between neurons and glial cells is important. Here we studied transgenic knock-in mice carrying a familial hemiplegic migraine type 1 (FHM1) R192Q mutation (in the gene encoding a subunit of neuronal P/Q-type voltage-gated calcium channels) that display increased susceptibility to CSD, likely because of increased glutamate and K\(^+\) in the extracellular milieu. Therefore, neuronal and glial signaling in FHM1 mice at the cellular level was investigated by measuring intracellular calcium, a cellular messenger that regulates a variety of physiological functions.

**Methods:** Neuronal and glial primary cell cultures of transgenic FHM1 mice and wild type littermate controls were loaded with fluorescent calcium indicator FLUO-4 AM and spontaneous calcium signaling, as well as in response to glutamate and K\(^+\), was visualized using confocal microscopy.

**Results:** Neurons of FHM1 mice displayed altered spontaneous calcium signaling as well as in response to KCl and glutamate. Preliminary data in glial cells suggests also alterations in calcium signaling in glial cells of FHM1 mice.

**Conclusions:** Differences in neuronal calcium signaling may be correlated to increased neurotransmitter release and increased sensitivity of mutant mice to hyperexcitability and CSD. Differences in glial calcium signaling may be attributed to long-term effects of more frequent exposure to high levels of K\(^+\) in vivo. These results seem to indicate that changes in both neuronal and glial signaling may play a role in FHM1 mechanisms.

**PS1-117**

**Increased prevalence of migraine with aura in marfan syndrome is disease severity dependent**

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**Purpose:** To assess the lifetime prevalence of migraine in patients with Marfan syndrome (MFS) with or without aortic root replacement (AR) as a measure of disease severity.

**Methods:** In a multicenter study 123 MFS patients (mean age 42 y. SD 14, 43% male), 82 age and sex matched controls (43 y. SD 15, 38% male), and 51 non-MFS patients with a history of AR (53 y. SD 15, 77% male) were administered a semi-structured headache questionnaire. Migraine diagnose was made by a neurologist blinded for MFS-status. Multivariate models adjusted for age and gender were used.

**Results:** Life time prevalence of migraine with aura (MA), but not without aura, was increased in MFS patients (25% vs. 10% in controls; OR adjusted for age and gender; 3.3 [95%CI 1.4-7.7]). In a logistic multivariate regression model using all diagnostic groups with controls set as reference group (OR 1.0), the OR of having MA for the non-MFS group with AR was 2.7 [0.9-8.5], for the MFS group without AR 2.3 [0.9-2.9] and 5.5 [2.1-14.5] for the MFS group who underwent AR.

**Conclusion:** The lifetime prevalence of MA, but not migraine without aura, was increased in MFS, in particular in more severely affected patients who underwent AR. The prevalence of MA was also increased in non-MFS patients who underwent AR. This study adds to the evidence that cardio-vascular disease mechanisms are associated with migraine with aura.

**PS1-118**

**Genetic polymorphisms of the renin-angiotensin-aldosterone system in japanese patients with migraine**

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**Objectives:** The pathophysiology of migraine has not yet fully understood but may involve painful vasodilatation of cerebral blood vessels. One of the angiotensin-converting enzyme (ACE) inhibitor, lisinopril, and the angiotensin II receptor blocker candesartan respectively provided effective migraine prophylaxis with randomized controlled trials. These trials suggested that the renin-angiotensin-aldosterone (RAA) system must be concerned at least in part with the pathogenesis of migraine. ACE is one of the key enzymes in the RAA system, which modulates vascular tension and blood pressure. We have previously reported that insertion (I) / deletion (D) polymorphism in the ACE gene may be a genetic risk factor for migraine. This study was designed to determine the prevalence of common polymorphisms in the RAA system among Japanese patients with migraine.
Methods: This study consisted of 49 patients suffering from migraine with aura (MA), 114 from migraine without aura (MO), and 170 non-headache healthy controls. Genotyping for ACE I/D, angiotensin receptor 1 (AGTR1) A1166C, and angiotensinogen (AGT) Met235Thr polymorphisms were performed on leukocyte genomic DNA samples by polymerase chain reaction. We conducted multivariate analysis: p < 0.05 was considered to be significant.

Results: After adjusting for age and sex, only ACE D/D genotype was significantly associated with MA (p = 0.018). After adjusting for age and sex, no genotyping was associated with MO.

Conclusions: Our results support the conclusion that the ACE gene may be a genetic risk factor for MA.

PS1-119
A modularized managed care program for chronic headache
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Patients with primary headaches are often undertreated. A managed care program (MCP) enables low thresholds for referral, no treatment of non- or less chronified headache patients, treatment according to guidelines considering severity and chronicity of headache.

Objective: To analyze characteristics, disability and health-related quality of life (HRQL) as well as psychiatric comorbidity for validation modules of MCP.

Methods: Patients suffering from primary headaches in part with medication overuse were assessed by neurologists, psychologists and physical therapists. Questionnaires assessing mood (HADS), headache-related disability (MIDAS), health-related quality of life (SF-12) and chronic pain grading (v.Korff) were used. Patients were assigned to one of four treatment modules due to headache frequency, medication overuse and psychiatric comorbidity. Patients are referred back to headache specialists.

Results: 567 patients were included (43.2 years, female: 90.9%, duration of disease: 20.7 years). ICHD-II diagnoses were: migraine (n=283); tension-type headache (n=53), migraine + others (i.e. MOH, n=203), cluster headache (n=28). Headache frequency was 10.1 days/month and varied significantly across MCP-modules (2.84 “no chronicity”, 7.6 “moderate chronicity”, 12.4 “severe chronicity” and 16.2 “very severe chronicity, additional problems”); (F(3,563)12.41;p< 0.001). Mean medication/month was 6.4, differing significantly (3.0/4.3/5.7/19.1;F(3,561): 56.15,p< 0.001). MIDAS-score (18.5/33.8/62.7/88.1) and severity of chronic pain (v.Korff): 1.82/2.33/2.61/2.94(p< 0.001)) also differed significantly. 46.7% of patients displayed psychiatric comorbidities. HRQL and MIDAS was significantly higher in patients with than without psychiatric comorbidity (F(3,563)42.24;p< 0.001).

Conclusions: Chronic headache patients in a MCP present headache-related disabilities. We demonstrate that the modularized program allows a discrimination between patients according to severity and chronicity of their headaches.

PS1-120
Is the erythrocytic magnesium level a predictor for efficacy of oral magnesium in migraine prophylaxis?
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Background: Recommendations of magnesium for migraine prophylaxis focuses on a small number of studies. Intercellular intraerythrocytic magnesium levels were decreased in migraine sufferers. We were interested in the prophylactic efficacy of magnesium in migraine. Moreover, we recorded intraerythrocytic magnesium levels to predict the outcome of migraine prophylaxis.

Methods: In this prospective, placebo-controlled, double-blind randomized study, 55 patients with migraine (2 to 6 migraine attacks/month) according to IHS criteria (76.8% female, mean age 36.8 years, BMI 23.1; n=34 (60.7%) migraine without aura, n=6 (10.7%) migraine with aura, n=16 (28.6%) migraine + tension-type headache) participated. After baseline, treatment with magnesiumoxide (148.8 mg=6.2 mmol 3times daily =18.6 mmol/day) or placebo was followed (28 received magnesium, 27 placebo). Intraerythrocytic magnesium levels were detected by atomic absorption. The primary end-point was reduction of at least 65% in intensity or duration of migraine attacks.

Results: The percentage of responders (intensity/duration of migraine attacks) was 55.0%/54.5% in the verum
and 55%/50% (n.s.) in the placebo group. Intraerythrocytic magnesium levels were 2.19 ± 0.3 / 2.14 ± 0.33 mmol/l in the verum/placebo group (n.s.) at run in phase and 2.07 ± 0.23 / 2.08 ± 0.31 mmol/l (n.s.) after 16 weeks. The correlation between the intensity/duration of migraine attacks and the red blood cell magnesium level was -.299 (n.s)/-.005 (n.s).

Conclusions: Our results confirm earlier findings who couldn’t demonstrate any prophylactic effect of 10 mmol magnesium twice-daily for migraine prophylaxis. Additionally we recorded normal intraerythrocytic magnesium levels in migraineurs. There were no significant differences between pre and post.

PS1-121
Preventive migraine medication and electroencephalographic changes
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Purpose: To establish any correlation between preventive treatment of migraine and electroencephalographic (EEG) changes.

Patients and methods: The study was conducted prospectively on 45 patients diagnosed with migraine. The diagnosis is established according to ICDH II. The mean age was 39.2 years old. There were 37 (82.2%) females and 7 (17.8%) males. The imaging resulted normal for all of them. Two EEG are recorded before beginning and 6 weeks after using the preventive treatment for each patient. The treatment with flunarizine hydrochloride (up to 10 mg once day) and tricyclic antidepressants (amitriptyline) (up to 50 mg once daily) is used.

Results: We analyzed the EEG wave patterns before and after medication. There were 21 normal registrations (18 females, 3 males) at the beginning resulting normal even at the second registration. The other patients had wave pattern anomalies (mainly beta activity and sometime theta activity). No correlation between gender and migraine classification is found. The frequency of headache was higher to the patients presenting EEG changes. No significant changes are found between the EEG records before and after medication, independently of clinical effect of the used treatment.

Conclusion: The EEG is not influenced by the preventive treatment used for migraine.

PS1-122
Onabotulinum toxin, type a, [bonta]: treating co-morbid chronic migraines and temporo-mandibular dysfunction [tmd]
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We tested the efficacy/safety of using onabotulinum toxin, type A, [BontA] in the treatment of TMD co-morbid with chronic migraines. [CM], > 15 per month. We now studied patients that met IHS criteria for chronic migraine (CM) along with chronic TMD.

56 patients (43 = f, 13 = m) were studied who fulfilled TMD and chronic migraine IHS criteria. 100 units of BontA were used to treat each patient using an intradermal injection technique of administration. Average age of patients was 39.4 years of age (range = 21-72 yrs). 54% were unilateral in symptoms; the rest were bilateral. Patients kept migraine and pain diaries, using a 0-10 score for rating their symptoms and were seen monthly after BontA injection over a period of 3 mos.

Decreases in TMD pain and clenching were 72.5% with results lasting 9.5 weeks (range = 4-21 weeks); corresponding decrease of CM frequency of almost 80%. An average of 18.6 migraines per month reduced to approximately 4 migraines per month, lasting an average of 12.5 weeks (range = 6-38 weeks). No side effects of BontA injection were reported.

BontA used intradermally to treat TMD/CM symptoms is efficacious and reduced frequency of associated migraines/migrainous headaches in our patients. We conclude that BontA can be useful to reduce TMD pain and co-morbid migraines and this activity is likely in trigeminal pathways. These preliminary results should be further studied in a more rigorous double-blind manner.

PS1-123
Iv tramadol treatment for chronic daily headache [cdh] and new daily persistent headaches [ndph] in the outpatient clinic
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We studied the efficacy and safety of treatment of CDH and NDPH with IV tramadol in an outpatient headache clinic setting.
Tramadol is indicated for pain but is not available in the US in an IV form. We prepared a sterile injectable form of tramadol.

24 patients with CDH (n = 18f, 6m) and 10 patients with NDPH (n = 7m, 3f) were treated with IV tramadol in the clinic. CDH patients had headaches for an average of 6.1 years and NDPH patients for 2.9 years. 50-100mg were given by IV push every 15 minutes. Patients and staff monitored reductions on a 0-10 point scale.

Beginning severity of CDH was 7.1/10; for NDPH it was 6.8/10. After treatment, CDH severity was 2.2/10, with 7 patients reporting no headache at all (p < .001). NDPH severity reduced to 2.5/10 with 2 patients reporting no headache at all (p < .02). Reduced severity (at least 50%) of CDH/NDPH was 18.9 hours (range 6.5-36 hours). Dose of tramadol was 468 mg, over 2.2 hours. 3 patients experienced nausea; 4 experienced drowsiness.

Tramadol, given IV, can rapidly and safely reduce severity in CDH/NDPH, without toxicity. The rapidity with which tramadol acts when given IV is far faster in time course/degree compared to oral dosing and may relate to extent of penetration of tramadol into the CNS or may reflect re-uptake inhibition of serotonin and norepinephrine or a rapid effect on mu opioid receptors, or both, in the CNS. Double-blind studies are warranted.

IV baclofen is a safe and efficacious treatment for refractory migraines/headaches associated with muscle spasm in an outpatient setting with monitoring. This is another unique approach to treatment, where active treatment is provided. Side effects were minimal; double-blind studies for this medication are definitely warranted, given the impressive initial open-label results. Baclofen, type B receptors in the maintenance of migraines and spasm is postulated.

Alterations of microglia and astrocytes in the trigeminal nucleus caudalis by continual trpv1 stimulation on the trigeminal nociceptors


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Background and aims: TRPV1 (transient receptor potential vanilloid subfamily 1) is a capsaicin-sensing receptor, which is known to be distributed in the sensory systems. Continual noxious stimulation at the peripheral sensory terminals is reported to cause the activation of microglia and astrocytes in the spinal cord, and these findings are considered to be related to chronification of pain. In this study, to investigate the mechanism of migraine chronification, we stimulated TRPV1 on the trigeminal nociceptors, and observed the change in the numbers and localization of microglia and astrocytes in the trigeminal nucleus caudalis (TNC).

Methods: Sprague-Dawley rats were divided into three groups. Capsaicin(10mM,100μl) was injected in the left face for two days(d2-group), four days(d4-group) or six days(d6-group). As control(c-group), vehicle was injected in the left face for two days. After the last injection, TNC was removed and processed for immunohistochemistry. To detect the microglia and astrocyte, anti-Iba-1 and anti-GFAP antibodies were used, respectively. For quantification, the ratio of area immunoreactive for Iba-1 or GFAP was calculated in serial eight sections.
Results: The ratio of area immunoreactive for lba-1 was significantly increased in d2-group (23.7%) compared to c-group (7.3%; p < 0.01) on the injected side. The ratio of area immunoreactive for GFAP in d2 (15.1%) and d4-group (13.8%) also showed a significant increase compared to c-group (7.3%; p < 0.01) on the injected side.

Conclusion: Continual TRPV1 stimulation on the trigeminal nociceptors increases microglia and astrocytes activities in the TNC, which might be related to the chronification of headache.

PSI-127
The effect of sumatriptan and telcagepant on cgrp-induced dilatation in human isolated middle meningeal arteries

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The neuropeptide Calcitonin Gene-Related Peptide (CGRP), playing an important role in migraine, is a potent dilator in human cranial arteries. It is still under debate whether the main effect of CGRP is central or peripheral. Sumatriptan reverses the dilatory effect of CGRP by constricting cranial arteries, whereas telcagepant normalizes dilated vessels by blocking the CGRP receptor. Since most patients take antimigraine drugs after the attack has started, this study investigated the effects of sumatriptan and telcagepant in Human isolated Middle Meningeal Arteries (HMMA’s) after dilation of these vessels with CGRP. HMMA’s were obtained during frontal brain surgery (3M,2F;39-76yrs). After preconstriction with KCl (30mM) the arteries were dilated with exogenous CGRP. HMMA’s were obtained during frontal brain surgery (3M,2F;39-76yrs). After preconstriction with KCl (30mM) the arteries were dilated with exogenous CGRP. HMMA’s were obtained during frontal brain surgery (3M,2F;39-76yrs). After preconstriction with KCl (30mM) the arteries were dilated with exogenous CGRP.

Conclusions: Sumatriptan or telcagepant was added to the arteries in concentrations corrected for plasma protein binding. Thus, reversal of vasodilation in HMMA’s shows that both sumatriptan and telcagepant are capable of reversing the dilation induced by CGRP, even when the concentration is corrected for plasma protein binding. Thus, reversal of vasodilation in the meningeal artery is one of the possible modes of action of sumatriptan and telcagepant.
**PS1-128**

**Mass spectroscopy (seldi) analysis of serum biomarkers in patients with migraines and paroxysmal headaches**

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Beta-3 subunit of G proteins (GNB3) as a product of serotonin transporter gene polymorphism seems to be a valuable biomarker of many headaches, including paroxysmal cluster headaches. The aim of our research was to evaluate the level of GNB-3 in the serum of patients with different cephalalgia forms, including migraines and paroxysmal headache. Under our observation were 124 patients (84 females and 40 males) with migraine and 108 patients (69 females and 39 males) with paroxysmal headaches. Control group consisted from 235 healthy donors without any type of cephalalgia. Surface-enhanced laser desorption/ionization (SELDI) is an ionization method in mass spectrometry that is used for the analysis of protein mixtures. SELDI is typically used with time-of-flight mass spectrometers and is used to detect proteins in tissue samples, including blood serum. The patients were treated by standard therapy: Aspirin, Ibuprofen, Naproxen, and Reglan. We investigated the GNB3 serum levels in both patient's and control groups. It was found that the GNB3 level was considerably higher in patients with different cephalalgia forms in comparison with healthy donors. After 3 months of standard treatment, the GNB-3 levels decreased in most patients with migraine and in almost half of paroxysmal headache patients.

It is well documented the relationship between GNB3 polymorphism and hypertension, insulin resistance. The possible future research could elucidate mechanisms of GNB3 polymorphism action nociceptive mechanisms on different cephalalgias and some genetic predispositions for response on treatment and long term prognosis in patients with migraines and paroxysmal headaches.

**Background:** The stepped-care approach to migraine management uses symptomatic treatments such as aspirin as first-line and reserves triptans as second-line treatment for those in whom this has proved ineffective. Stratified care chooses between symptomatic therapy and triptans as first-line treatment, doing so on an individual basis according to perceived illness severity. We questioned the two assumptions underpinning stratified care: that greater illness severity reflects greater need and that greater severity is a risk factor for failure of symptomatic treatment but not of triptans.

**Methods:** We reviewed individual patient data from six relevant clinical trials of aspirin 1000 mg in migraine (N=2,079; 1,165 moderate headache, 914 severe) and one of aspirin 500 mg and 1000 mg in episodic tension-type headache (ETTH) (N=325; 180 moderate, 145 severe), relating outcome to pre-treatment headache intensity.

**Results:** In migraine, for headache relief at 2 hr, only a small (4.7%) and non-significant risk difference (RD) in a therapeutic gain (TG) favoured moderate pain; for pain-freedom at 2 hr, TGs were almost identical (RD: -0.2%). In ETTH, for headache relief at 2 hr, RDs for both aspirin 500 mg (-4.2%) and aspirin 1000 mg (-9.7%) favoured severe pain, although neither was significant; for pain-freedom at 2 hr, the respective RDs (-14.2 and -3.6) again favoured severe pain.

**Conclusion:** In neither migraine nor ETTH does pre-treatment headache intensity predict success or failure of aspirin. This is not an arguable basis for stratified care in migraine. In both disorders, aspirin is first-line treatment regardless of headache intensity.

**PS1-130**

**The eurolight project: highlighting the impact of primary headache disorders in Europe - description of methods**

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Background: The EUroLight project is the first at European Union level to assess the impact of headache disorders, and also the first project of its scale performed by a collaboration between professional and lay organizations and individuals. The project took the form of surveys by structured questionnaire, conducted from November 2008 to August 2009, of population samples from ten countries of Europe representing 60% of the adult population of the European Union.

Methods: Population-based were the surveys performed in Germany, Luxembourg, the Netherlands, Italy and Spain. In Austria, France and UK, samples were taken from health-care settings. Additionally in the Netherlands, Spain and in Ireland, samples were drawn from members of national headache patient organizations and their relatives. Independent double data-entry was performed in all cases.

Results: 9,269 correctly completed returned questionnaires were analysed. The questionnaires received had a moderate female bias (58%); of the respondents from the three patients’ organizations (n=992), 61% were female. The mean age of all respondents was 44 years; samples from patients’ organizations were slightly older (mean 47 years). The different sampling methods adopted in these ten countries worked with differing degrees of effectiveness, as evidenced by the responder-rates, which varied from 10.8% to 90.7%. In the population-based surveys, responder-rates varied from 11.3% to 58.8%.

Conclusion: The methodology, although with differences born of necessity in the various surveys in the ten countries, was sound overall, providing robust data revealing the amount of public ill-health that results from headache in Europe.

PS1-131
Exploring migraine susceptibility: positive results from an integrated study on multiple pathways

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In migraine pathophysiology, several mechanisms may lead to an abnormal activity of nociceptive pathways. Additionally, a neurogenic inflammatory reaction occurs with a vascular component associated. In this work, we studied candidate genes involved in some of these pathways, in order to identify genetic variants that might be associated with susceptibility to migraine with aura (MA) and without aura (MO).

A case-control approach was used, analysing 188 cases (111 with MO and 77 with MA) and 287 migraine-free unrelated controls.

We assessed the association between polymorphisms in STX1A and migraine since it is involved in neurotransmitter release. We confirmed the association of rs941298 and also found novel significant results for rs6951030. Regarding the vasoconstriction related gene, EDNRA, we determined that rs702757 is a susceptibility factor for MO, as previously reported; furthermore, we observed a trend towards an increased risk for MA, conferred by rs5333.

We also explored BDNF, a modulator of the trigeminal nociceptive plasticity and, for the first time, CGRP, a mediator of neurogenic inflammation, and a possible interaction between them. No significant main effects were detected, however a significant interaction between BDNF and CGRP was found.

In conclusion, rather than focusing only in one particular pathway we selected genes involved in several pathways, to gain a broader insight into migraine pathophysiology. The different mechanisms may be interconnected, and the variants found in each gene may contribute to susceptibility to migraine. These susceptibility variants can be used in the future as biomarkers and gene-gene interactions should be further explored.

PS1-132
Inhibition of meningeal nociceptors’ mechanosensitivity by botulinum neurotoxin type a (bonta): implications for migraine headache treatment

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Craniofacial injection of BoNTA has been shown to ameliorate chronic migraines, but the neurobiological underpinning of this effect is not known. Clinical data suggest that administration of BoNTA reduces the responsiveness of cranial nociceptive afferents. We therefore examined, using single unit recording from the trigeminal ganglia of urethane-anesthetized rats, whether BoNTA can inhibit the responsiveness of meningeal nociceptors, the primary afferent population whose mechanical activation is believed to mediate migraine pain. Given that some meningeal nociceptors send collaterals to the calvarial bone, we also examined the effect BoNTA on meningeal nociceptors with dual receptive fields, in the dura and calvaria. Local application of BoNTA (2 units over 1 hr) decreased the mechanosensitivity of 6/9 slowly-conducting C-units meningeal nociceptors and 1/8 faster conducting A-delta units. The onset of the inhibitory effect was delayed, and in most units was seen after 3-4 hrs. Local administration of BoNTA to the calvarial receptive field of meningeal nociceptors inhibited the mechanosensitivity in 3/3 C-units tested. None of the A-delta units tested was inhibited. Given that BoNTA is more effective in inhibiting migraine headache with an "imploding" characteristic, our data point to the inhibition of mechanosensitivity of slowly-conducting cranial nociceptors that dually innervate the meninges and calvarial bone as a potential mechanism through which BoNTA treatment prevents the onset of headache.

**PS1-133**

**Migraine, depression and chronic pain: a common etiology?**

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**Background and aims:** There is a fascinating relationship between migraine, depression and other pain conditions, possibly explained by shared underlying genetic factors. Here, we investigate whether migraine is associated with other pain conditions independent of its comorbidity with depression.

**Method:** We analysed data from the Netherlands Study of Depression and Anxiety (NESDA). Depression diagnoses were made with a CIDI interview (based on DSM-IV criteria). Migraine was assessed with questionnaire data based on ICHD-II criteria. In addition, participants were asked whether they had experienced pain in 7 different locations (back, neck, head, chest, joints, stomach, face) in the last 6 months.

**Results:** The sample included 970 individuals with no lifetime depression diagnosis, 789 with past depression and 1222 with current depression. A total of 1195 individuals had migraine or a milder form of migrainous headache. Individuals with current depression reported more pain sites (3.8 +/- 1.7) than individuals with past depression (3.1 +/- 1.7), or individuals with no lifetime depression diagnosis (2.5 +/- 1.6). Furthermore, migraine patients reported a larger average number of pain sites (headaches not included) than individuals without migraine (2.9 vs. 2.1, t=-12.9, p<.001). This effect remained significant when depression status was taken into account.

**Conclusion:** These results confirm the comorbidity of depression, migraine and other pain conditions, and suggest that the comorbidity of migraine and other pain conditions is at least partly independent of depression. Currently, similar data are being collected in a genetically informative sample to further study the etiology of these comorbidities.

**PS1-134**

**Is hemicrania continua absolutely responsive to indomethacin? Report of two cases successfully treated with pregabalin**

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**Objectives:** Hemicrania continua (HC) is an indomethacin-responsive headache. We report two cases fulfilling the ICHD-II criteria for HC, whose response to indomethacin was poor and not sustained, whereas was complete and prolonged to pregabalin.

**Materials and methods:** We have followed-up two male patients, 36 and 49 years old, respectively, suffering from HC.

**Results:** The 49-year-old patient presented when he was 45, and responded to indomethacin 150 mg/day. However, 4 months later, indomethacin efficacy appeared to fade and gastric discomfort was reported. Indomethacin was replaced by pregabalin, that was titrated to 600 mg/day, achieving pain-free status. Attempts to lower this dose resulted in return of headache within 14 days. The 36-year-old patient started suffering from HC three years earlier and was treated with indomethacin 200 mg/day. The headaches disappeared, but two months later the drug was discontinued due to gastric ache and subsequent evidence of ulcerative gastritis. Thereafter, the patient was commenced on pregabalin titrated to 300 mg/day, when he reported a pain-free condition. Attempts to lower dosage...
to 150 mg resulted in recurrence of continuous headaches. Discussion: The complete response to indomethacin is a prerequisite for HC diagnosis. Unfortunately, a proportion of patients develop gastrointestinal adverse effects that necessitate cessation of treatment. Moreover, sporadic unresponsive cases have been described.

Conclusions: Drugs other than indomethacin proved to be effective in HC. They include: anti-inflammatory agents (piroxicam β-cyclohexadrin and rofecoxib), verapamil, melatonin and anticonvulsants (topiramate, gabapentin, and valproate). This is the first report of responsiveness to pregabalin in the treatment of HC.

PS1-135
The treatment of hypnic headache: review of the literature including a personal new large case
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Objectives: Hypnic headache (HH) is a primary headache, which occurs exclusively during sleep. There are no controlled trials for the treatment of HH.

Materials and methods: We reviewed the 42 published papers, including 119 cases, which reported the response to medications used to treat HH. Moreover, we assessed the efficacy of therapy administered to 44 personally evaluated patients.

Results: HH was shown to respond to several medications. The drugs which were effective in at least 5 cases are: lithium, indomethacin, caffeine and flunarizine. However, the same medications provided no improvement in other patients. Lithium was the most extensively studied compound and demonstrated its effectiveness in 32 cases. In our case series caffeine, melatonin and indomethacin provided the best benefit.

Discussion: Lithium seems to be the first choice treatment for HH. Unfortunately, significant adverse effects are not rare, mainly in elderly patients. Many subjects reported a good response to indomethacin, but some could not tolerate it. Caffeine and melatonin efficacy was not consistently high as single preventive agents, but their association with lithium or indomethacin seemed to produce an additional therapeutic efficacy. Some patients responded completely to caffeine given alone.

Conclusions: A course of lithium should be tried first; if this treatment does not provide a significant response, as second line approach indomethacin can be commenced. If these treatments prove to be ineffective or poorly tolerated, other compounds, such as caffeine and melatonin, can be used. These drugs are also recommended when lithium and indomethacin are contraindicated or provoke adverse events.

PS1-136
Efficacy of frovatriptan in the acute treatment of menstrually-related migraine: analysis of a double-blind, randomized multicenter, comparative study vs. Rizatriptan
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Objectives: The aim of the study was to assess the efficacy of frovatriptan and rizatriptan in menstrually-related migraine in a subset of women participating in a multicenter, randomized, double-blind, cross-over study.

Materials and methods: Details on study design are available in a previous publication [1]. We retrospectively evaluated the subgroup of normally menstruating women who were enrolled for the trial [1]. The patients received frovatriptan 2.5 mg or rizatriptan 10 mg in a randomized sequence; they treated 3 attacks with each of study medications. Menstrually-related migraine was defined based on the criteria listed in the Appendix of ICHD-II [2].

Results: Out of the 125 patients included in the trial intention-to-treat analysis, 99 were females; 93 had regular menstrual cycles and were thus included in the evaluation. A total of 49 attacks classifiable as menstrually-related migraine were treated with frovatriptan and 59 with rizatriptan. Rate of pain relief at 2 hours was 58% for frovatriptan and 64% for rizatriptan (p = NS), while rate of pain-free at 2 hours was 31% and 34% (p = NS), respectively. At 24 hours, pain-free rates were 67% and pain relief 81% with frovatriptan, not significantly different (p = NS) from those obtained with rizatriptan (61% and 74%, respectively). Conversely, the recurrence within 24 hours was significantly lower (p < 0.01) with frovatriptan (9%), as compared with rizatriptan (18%).

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Conclusions: Frovatriptan was as effective as rizatriptan in the treatment of menstrually-related migraine attacks, in terms of pain-free and pain relief at 2 and 24 hours, but showed a lower rate of recurrence.

PSI-137
Association of 5-htt gene polymorphisms with migraine: a systematic review and meta-analysis
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Objective: It has been suggested that migraine has a strong genetic component. Serotonin is known to play an important role in the pathogenesis of migraine, but genetic association studies that examine the relationship between polymorphisms of serotonin transporter (5-HTT) gene and migraine have yielded inconsistent results. we conducted this systematic review with meta-analysis to evaluate the association between 5-HTT gene variants (including 5-HTTLPR, VNTR and SNP) and migraine.

Methods: We performed systematic review of studies that analyzed 5-HTT gene variants, and conducted meta-analysis of two or more studies that involved any variant of the 5-HTT. We analyzed the OR using a random-effects or fixed-effects model. Q statistic was used to evaluate homogeneity, and Egger’s test and Funnel plot were used to assess publication bias. For studies involving family-based association and linkage-analyses, a descriptive analysis was carried.

Results: A total of 15 studies were identified for meta-analysis. It was found that the 5-HTT VNTR Stin2.12 allele or 12/12 genotype had an increased risk for migraine in 495 cases and 729 controls in the general population (OR,95% CI: 1.34, 1.09-1.64, p = 0.006; 1.55,1.17-2.05, p = 0.002; respectively), but there was no significant association between migraine and 5-HTTLPR or SNP rs2020942.

Conclusions: Existing evidence indicates that the 5-HTT VNTR polymorphism (mainly the STin2.12 genotype) is associated with an increased risk of migraine in the general population. However, future studies with larger sample sizes will be necessary to confirm the present results.

PSI-138
Response to withdrawal therapy in clinical patients with medication overuse headache
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Objective: To study the response to withdrawal therapy in patients with medication overuse headache (MOH).

Background: MOH is a chronic disorder resulting from overuse of acute headache medications. Hitherto the evidence for withdrawal therapy is limited. There is some evidence that the success of withdrawal therapy depends on the underlying primary headache disorders.

Methods: We performed a retrospective study on withdrawal therapy in 249 outpatient MOH patients. Of these 249 MOH patients 50.2% overused analgesics, 5.2% triptans, 36.1% combination of both. Successful withdrawal was defined as a reduction in headache days of at least 50% after 3 months of acute withdrawal of all headache compounds and caffeine containing substances.

Results: Of the total population of 249 patients, 182 (73%) followed the advise of acute withdrawal and fulfilled the withdrawal period of 3 months. Of those who succeeded in the execution of the advise, 66 (36%) had a successful withdrawal. Among patients with underlying migraine (n=56), 60% had a successful withdrawal. Among patients with underlying tension type headache (n=48) or the combination of migraine and tension type headache (n=30), respectively 21% and 6% had a successful withdrawal.

Conclusion: Of all patients 73% did follow up the advise to acute withdraw medication. The chance on successful withdrawal is higher in migraine patients than in patients with tension type headache or with the combination of both.

PSI-139
Effect of gastrodin on calcitonin gene-related peptide expression in the rat trigeminal ganglion
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Aim: To explore the gastrodin pharmacological effects on migraine attack, the level of calcitonin gene-related peptide (CGRP) and extracellular signal-regulated kinase1/2 (ERK1/2) in rat trigeminal ganglion (TG) were observed after co-culture with gastrodin for 24 hours.

Methods: 2.5μM, 5μM, 10μM, 20μM, 40μM concentration of gastrodin were co-incubated with rat TG for 24 hours, respectively, then CGRP-immunoreactivity (CGRP-ir) positive cell were quantified by means of immunohistochemistry stain. Furthermore, the and CGRP-mRNA and phosphorylated ERK1/2 level was compared by method with western-blot and RT-PCR assay which after co-culture with ERK1/2 inhibitor PD98059, U0126 and effective concentration of gastrodin for 24 hours.

Results: 5μM and 10μM concentration of gastrodin concentration-dependently reduced of CGRP-ir positive cells number in rat TG which was comparison with 2.5μM, 20μM and 40μM concentration, and both concentration of gastrodin decreased significantly CGRP-mRNA and pERK1/2 level, but there was no difference between inhibitor PD98059, U0126 and gastrodin.

Conclusion: The optimal concentration of gastrodin remarkably reduce CGRP-ir, CGRP-mRNA and pERK1/2 level in cultured rat TG. We suggest that the gastrodin depress CGRP up-regulation by means of inhibiting intracellular signaling ERK1/2 pathway.

PSI-140
Propranolol efficacy in migraine prevention: assessing the role of different factors
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Objective: We performed an anteropospective study to assess the efficacy of propranolol in migraine prevention accounting different factors, including age, sex, blood pressure level, and duration of the disease.

Methods: Using The Migraine Disability Score Test (MIDAS), the study population consisted of 198 migraine patients, with no other headache variant, co-morbid illnesses or conditions that restrict the use of propranolol at standard doses for migraine prevention, selected. Then, therapeutic responses, including the frequency and severity changes, followed by 4 months, in 3 sessions (months 0, 2, and 4).

Results: The frequency (P-value= 0.0001) and severity (P-value= 0.003) of migraine attacks reduced significantly in individuals younger than 40. Frequency of attacks reduced more, in females than males (P-value= 0.0001). Besides, migraineurs with blood pressure levels, measured lower than 130/85 mmHg, had greater improvement at the end of study (P-value= 0.0001) for systolic BP level and severity change, and, also (P-value= 0.0001) for diastolic BP level and both severity and frequency changes. Individuals, suffered from migraine, more than five years, had greater response for overall severity reduction (P-value= 0.0001), and two months frequency decrease (P-value= 0.0001).

Conclusion: This study suggests that, propranolol maybe more effective to prevent migraine headaches, in individuals before age of 40, whose BP levels are lower than 130/85 mmHg, and also, with disease duration of five years or more. Furthermore, systolic blood pressure reduction is associated with the more severity and frequency improvement, while, diastolic BP reduction may predict, only, better severity improvement.

PSI-141
Total migraine freedom: a potential primary endpoint to assess acute treatment of migraine in the avitriptan program
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Background: FDA currently requires four co-primary endpoints, at 2 hours post-dose, to establish efficacy in migraine patients. Total migraine freedom (TMF; pain free and no associated symptoms of photophobia, phonophobia and nausea) has been proposed as an alternative primary endpoint. TMF represents a single composite endpoint that is easier to translate into clinical practice and was demonstrated to have significant advantages versus the standard four co-primary endpoints (Rogers et al; 2010). This analysis investigates TMF using an avitriptan (discontinued in 1997) clinical trial data base.

Methods: Retrospective data analysis of 5 double-blind placebo-controlled studies of avitriptan in the treatment of acute migraine. TMF at 2 hours was evaluated using the CMH test statistic in pairwise comparisons to placebo. Simulation studies utilizing bootstrap sampling from the pooled data of the five studies were used to compare the empirical power of the TMF approach versus the four co-primary endpoints.
**Results:** Odds ratio (avatriptan vs. placebo) for TMF were 6.19 [95% CI: (3.99, 9.61), \( p < 0.001 \)]. The proportion of patients achieving TMF at 2 hours for avitriptan and placebo were 30% and 6%, respectively. Simulation results showed a substantial loss in power in the four co-primary endpoints approach versus the composite TMF endpoint.

**Conclusion:** Avitriptan was superior to placebo in achieving TMF at 2 hours post-dose. Given that the majority of patients with migraine did not present with all three associated symptoms at baseline, the TMF endpoint has significant advantages as a primary endpoint compared to establishing efficacy with four co-primary endpoint.

**PS1-142**

**The mechanism of angiotensin ii toward cortical spreading depression in migraine model rat**

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**Background and aims:** Angiotensin II receptor inhibitors (ARBs) are known to prevent migraine attack, but its mechanism is unclear. Cortical spreading depression (CSD) is also known to correlate with migraine. The aim of this study is to elucidate the mechanism of ARB in rat CSD model.

**Methods:** 23 male Sprague-Dawley rats, weighing 350-600g, were anesthetized and ventilated mechanically. Parietal cortical blood flow (CoBF) was monitored with a laser-Doppler flowmeter. A hydrogen electrode was placed trough cranial window to measure parietal direct current potential (DCP). CSDs were induced with application of 3\( \mu \)l of 1M KCl solution through another cranial window. In control group (\( n = 5 \)), CoBF and DCP were monitored two times for 60 minutes in order to measure CSDs. In Angiotensin II (Ang II) group (\( n = 7 \)), 2nd CSDs were induced with continuous intravenous administration of 50ng/kg/minutes of Ang II. In Ang II + ARB group (\( n = 5 \)) and Ang II + CCB group (\( n = 6 \)), CSDs were recorded in the same way as Ang II group after administration of 100\( \mu \)g/kg of olmesartan or 100\( \mu \)g/kg of nifedipine.

The data were analyzed by Dunnett’s method.

**Results:** In Ang II group, the frequency of 2nd CSDs was increased by 182% compare with 1st CSDs significantly (\( P < 0.05 \)). Conversely, no significant change was observed on 2nd CSDs in control group (117%), Ang II + ARB group (112%) and Ang II + CCB group (87%).

**Conclusions:** Our results indicate that Ang II may have a role in migraine attack through Ang II receptor and voltage gated calcium channel.

**PS1-143**

**Onabotulinum toxin-a in chronic migraine (cm); 10 years experience in 376 patients evaluated prospectively**

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**Objective:** To report prospectively evaluated 10 years experience with Onabotulinum Toxin-A in 376 patients with Chronic Migraine (CM), including efficacy based on disability (MIDAS), average duration and onset of action, influence on acute medication use, effects of repeated long term use, adverse events, tachyphylaxis and certain predictors of positive and poor responses.

**Design/methods:** Evaluations of CM patients included, MIDAS scale, alldynia questionnarie, Beck Anxiety and Depression Scales, Mood Questionnaire, and Headache diaries. Using Fixed Sites and follow the pain protocol, 100 units of Onabotulinum Toxin-A were given initially and during repeat injections. Poor responders were given at least one more chance for repeat injection.

**Results:** Number of Onabotulinum Toxin-A treatments ranged from one to sixteen per patient. Based on fifty percent or more reduction in the MIDAS scale seventy-one percent of patients were considered responders. Average time of onset was twelve days (7-21 days). Average duration of effect was twelve weeks (8-22 weeks). Use of acute medications was significantly reduced in responders. Number of severe migraine attacks diminished and the ER visits went down to insignificant numbers. Predictors of good response included predominantly unilateral migraine and presence of scalp allodynia. Poor responders had predominant tension type headaches, severe depression, significant cyclothymia, severe and unusual stressful events and borderline personalities. Tachyphylaxis occurred in four patients. Transient drooping of the eye lids (12%), injection site pain (3%), generalized aches and pains (1.5%), and atrophy of the anterior Temporalis muscles (3%) were adverse events.

**Conclusions:** Long term treatment with Onabotulinum Toxin-A in CM reduces disability and acute medication use and is safe.
PS1-144

Anti-nociceptive and anti-inflammatory activities of the hexane and ethyl acetate extracts of CROTON MACrostachyUS stem bark in rats and mice

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The hexane and ethyl acetate extracts of the stem bark of Croton macrostachyus (family Euphorbiaceae) was investigated for possible anti-nociceptive and anti-inflammatory effects in mice and rats. Three models were used to study the extracts effects on nociception which were the acetic acid-induced abdominal constriction test, formalin test (both in mice) and the algameter test in rats. The anti-inflammatory effects were investigated employing the carrageenan-, histamine-, serotonin-, and formalin-induced hind-paw oedema in rats. Results of the study revealed the extracts to have significant (\( P < 0.001 \)) anti-nociceptive effect at a dose of 600 mg/kg p.o. in mice and rats in all the models for anti-nociception while 300 mg/kg p.o. showed significant (\( P < 0.001 \)) effect in the acetic acid-induced abdominal constriction test and in the formalin test. The two extracts also exhibited acute and chronic anti-inflammatory effects which were found to be significant (\( P < 0.001 \)) at 600 mg/kg p.o. in the rats tested. Preliminary phytochemical screening of the extract showed the presence of alkaloids, terpenoids and phenolic compounds in the hexane extract; whereas the ethyl acetate extract showed the presence of flavonoids, terpenoids and phenolic compounds. The results suggest the extract contains pharmacologically active principles. The result is in agreement with the local application of the plant in painful and inflammatory conditions.

PS1-145

Visual and auditory perceptual rivalry in migraine

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Background and aims: Perceptual rivalry refers to regular fluctuations between “competing” perceptual states that are induced by ambiguous stimuli - stimuli that can be validly perceived in more than one way. The most commonly studied perceptual rivalry examples are visual: for example, the Necker cube and binocular rivalry. However, perceptual rivalry also exists in the auditory and tactile domains. Recent studies show that perceptual rivalry rate can be modulated by perturbation of the serotonergic system in healthy observers. Specifically, pharmacologically lowering the availability of serotonin results in slower rivalry rates. As it has been suggested that brain serotonin is low during the interictal phase of migraine, we hypothesized that perceptual rivalry rates would be reduced in individuals with migraine.

Methods: We obtained measures of both visual and auditory rivalry in a group of 30 people with migraine (15 with aura; 15 without aura) while they were symptom free, and 20 approximately age-matched non-headache controls.

Results: Our experiments revealed fewer perceptual rivalry switches within both visual and auditory domains for our migraine without aura group (\( F(2,46) = 4.12, p=0.02 \)), while the with-aura group performed similarly to non-headache controls. Dividing the data by headache frequency rather than headache subtype classification revealed slower perceptual rivalry switching in those with more frequent headaches (\( F(2,46) = 6.14, p < 0.01 \)).

Conclusions: Our data provides further support for interictal differences in brain sensory activity in migraine, with the observed effects being in the same direction as those caused by pharmacologically reducing brain serotonin availability in normal observers.

PS1-146

A drug interaction study assessing the effects of cyp3a4 inhibition on the pharmacokinetics of levadex™ (map0004 orally inhaled dhe) in healthy volunteers

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Objective: Assess impact of CYP3A4 inhibition on LEVADEX™ (MAP0004, orally inhaled DHE) pharmacokinetics.

Background: Currently dihydroergotamine (DHE) requires a label warning about serious drug interaction when co-administered with CYP3A4 inhibitors as it is thought to potentially enhance the serum concentrations of DHE. However, no study has documented such effect.

Methods: Phase I open-label study. Twenty-four subjects were evaluated in a cross-over design: MAP0004 (1.0 mg) dosing was followed by MAP0004 co-administered with...
ketoconazole (400 mg once/day for four days), which was followed by 1.0 mg IV DHE. Pharmacokinetics following the three treatments were determined for both DHE and its metabolite 8c-hydroxydihydroergotamine (8c-OH DHE).

Results: The DHE Cmax geometric means were 2,583 pg/mL after MAP0004, 2,495 pg/mL after MAP0004 co-administration with ketoconazole, and 27,771 pg/mL after IV DHE administration. The Cmax, AUC0-48, AUC0-inf, and bioavailable fraction were not significantly different between MAP0004 alone and MAP0004 co-administered with ketoconazole. The half-lives were similar, in both with a geometric mean of 13.5 hours and 11.2 hours, respectively.

The 8c-OH DHE Cmax geometric means were 69 pg/mL after MAP0004 administration, 80 pg/mL after co-administration with ketoconazole, and 303 pg/mL after IV DHE administration. No significant difference in Cmax was observed between the two. A significant difference in 8c-OH DHE AUC0-48 and AUC0-inf was observed between MAP0004 and MAP0004 co-administered with ketoconazole, but levels of 8c-OH DHE were too low to be pharmacologically relevant.

Conclusion: There was no apparent effect of CYP3A4 inhibition on MAP0004 Cmax or elimination.

Study supported by: MAP Pharmaceuticals, Inc.

PS1-147
Assessment of the consistency of pharmacokinetic parameters of levadex™ (map0004, orally inhaled dihydroergotamine) in healthy volunteers - results from 3 clinical studies

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Objective: To assess pharmacology of LEVADEX™ (MAP0004, orally-inhaled dihydroergotamine (DHE)) across three clinical studies.

Background: Rapid and consistent absorption of a drug is important for effectively treating migraine acutely. MAP0004, a novel, orally-inhaled DHE, has been shown to effectively treat a migraine acutely. Data from three separate pharmacokinetic (PK) studies is analyzed to assess consistency, adequacy, and speed of absorption of DHE through this new route of administration.

Methods: Three studies compared MAP0004 1.0 mg nominal to 1.0 mg of IV DHE. One assessed the difference in PK between smokers and non-smokers, a second study assessed the effect of co-administration of ketoconazole on MAP0004, and the third assessed acute effects of MAP0004 on pulmonary artery pressure.

Results: MAP0004 delivered DHE rapidly in all three studies, with a Tmax mean range of 7-11 minutes. Peak plasma concentration of DHE was consistent across studies in non-smokers, with a Cmax geometric mean range of 2475-2551 pg/mL.

MAP0004 Cmax values were significantly lower than those for IV (average Cmax of ~45,000 pg/ml) but generally higher than those reported for intranasal administration (1,004 pg/ml). Cmax and clearance did not vary significantly based on lung function, age, or weight across studies. Co-administration of ketoconazole did not significantly impact MAP0004 PK.

Concentrations of 8c-hydroxy-dihydroergotamine after MAP0004 administration were low (average Cmax of <100 pg/ml). No unique MAP0004 tolerability issues were observed.

Conclusion: Across these studies MAP0004 showed consistent pharmacokinetic results and rapid absorption via the pulmonary route of administration.

Study supported by: MAP Pharmaceuticals, Inc.

PS1-148
Trigeminal neuralgia induced dystonia

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Background: Trigeminal neuralgia is considered one of the most painful episodes with several seconds of sharp, lancinating pains across one of more branches of the trigeminal nerve. Dystonia is a prolonged motor disorder where muscles may repetitively contract or posture into abnormal positions. Oromandibular dystonia is one form of focal dystonia affecting the muscles of mastication, facial expression and the tongue.

There are increasing case reports in the literature reporting Botulinum toxin injections alleviating the pains associated with trigeminal neuralgia. Botulinum toxin blocks
release of acetylcholine at the neuromuscular junction reducing the ability for the affected muscle to contract. As of this writing Botulinum toxin injections are not indicated for the management of trigeminal neuralgia.

Methods: A case series of four individuals with oromandibular dystonia secondary to trigeminal neuralgia is reviewed.

Results: This limited case series suggests benefit to muscular restriction however the relief of neuralgia pain is of debate.

Conclusion: In individuals with classic trigeminal neuralgia and secondary muscular contraction consistent with oromandibular dystonia, the Botulinum toxin injections may be able to assist in the muscular component to pain allowing for an increased range of mouth opening, however from these isolated case reports it is unknown if Botulinum toxin is helpful at addressing neuralgia type pain. Further study is needed to determine if Botulinum toxin can in fact reduce and address neuralgia pains and episodes, but it is likely able to reduce muscle spasm secondary to the severe lancinating pains of trigeminal neuralgias.

PSI-149

N-alpha methyl histamine, (histaminergic h3 agonist) versus propranolol in migraine prophylaxis: a randomized, double-blind study

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Objectives: To compare the efficacy and tolerability of the subcutaneous administration of N-alpha methyl histamine versus oral propranolol in the treatment of severe migraine attacks in migraine prophylaxis, undertaking a double-blind, placebo-controlled study.

Background: N-alpha methyl histamine has a selective affinity for H3 receptors and it may specifically inhibit the neurogenic edema involved in migraine, and could constitute a new therapeutic drug in migraine prophylaxis. Propranolol proved effective in migraine preventive therapy.

Methods: Sixty patients with migraine with or without aura were selected and enrolled in a 12-week double-blind controlled clinical trial to evaluate the efficacy of subcutaneous administration of N-alpha methyl histamine (1 to 3 ug twice a week) n=30, compared to administration of 120 mg/day of oral propranolol n=30. The variables studied were: headache intensity, frequency of attacks, duration of migraine attacks, MIDAS and analgesic intake.

Results: Fifty five patients completed the study. The data collected during the 4th week of treatment revealed that N-alpha methyl histamine and propranolol caused a significantly (p< 0.01) greater reduction between the basal values and final values of every variable studied.

Conclusions: This randomized study demonstrated that both N-alpha methyl histamine and propranolol are similarly effective and well tolerated in reducing or eliminating the headache in migraine prophylaxis. Low doses of N-alpha methyl histamine applied subcutaneously may represent a novel and effective therapeutic alternative in resistant migraine patients and may lay the clinical and pharmacological groundwork for the use of H3 agonist in migraine prophylaxis.

PSI-150

Immunohistochemical localization of the clr/ramp1 receptor complex in the trigeminovascular system of the cynomolgus monkey

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Calcitonin-gene-related peptide (CGRP) is implicated in the pathophysiology of migraine due to its potent vasodilatory effects. To understand the role of CGRP mediated signaling in migraine, we mapped CGRP receptor localization in relation to CGRP peptide expression in the trigeminovascular system of the cynomolgus monkey. To ensure specificity and overcome the technical and interpretational challenges of co-localization experiments with polyclonal antibodies raised against individual components of the receptor, we used a monoclonal human IgG1 antibody that specifically recognizes the CLR/RAMP1 heterodimer.

We show that this antibody is specific for the heterodimeric CLR/RAMP1 receptor complex, both in cell lines expressing the receptor versus controls and in tissue versus a pre-absorption or non-CGRP receptor control antibody. In the trigeminovascular system of the cynomolgus monkey, CGRP receptors are expressed on multiple levels: Immunoreactivity was localized in the dural vasculature, neurons and satellite cells in the trigeminal ganglion and neurons in the spinal trigeminal nucleus. Furthermore, immune-electron microscopy studies show that the
expression in the spinal trigeminal nucleus is postsynaptic to CGRP containing terminals.

These data reinforce and clarify our understanding of CGRP receptor localization in a pattern consistent with a role for CGRP in trigeminal vascular sensitization, and provide additional evidence that interfering with CGRP receptor transmission is beneficial for the treatment of migraines.

**PS1-151**

**Autonomic interoceptive disorders profile in chronic migraine**

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**Background and aims:** Recently new concepts were developed about the pain as a homeostatic emotion (Craig A.D., 2003) and autonomic interoceptive afferent pathways (Janig W., 2009). The aim of this study was to analyze the autonomic interoceptive sensations in patients with chronic migraine (CM).

**Methods:** Three groups of patients (all females) were studied:

1 group - 38 patients with CM, average age 37.3 years;

2 group - 28 patients with generalized anxiety disorders (GAD) without migraine, average age 35.2 years;

3 group - 27 healthy subjects, average age 38.1 years.

An original questionnaire (Moldovanu I., Vovc V., 2010) to determine the profile of autonomic interoceptive disorders (PAID) was used. PAID includes 8 related to autonomic interoception scales (breathlessness, dizziness, feeling faint, cardio-vascular, gastro-intestinal, sexual, menstrual, algic) with 102 items.

**Results:** Most of PAID scales results were significantly different in patients with both CM and GAD groups in comparison with healthy group. PAID parameters had higher values in CM than in GAD patients, but statistically significant differences between those 2 groups were found only at following scales: breathlessness (14.5±0.5 vs. 10.5±0.4; p< 0.05), cardiovascular dysfunction (29.1±0.3 vs. 23.3±1.9; p< 0.05) and musculoskeletal pain (10.2±0.1 vs. 7.3±0.4; p< 0.05).

**Conclusions:** CM pain and affective disorders have a lot of common autonomic interoceptive changes, but some interoceptive disorders are specific for CM. PAID seems to be a sensitive tool for clinical study and research of interoceptive disorders in CM patients.

**PS1-152**

**Drugs for preventing migraine headaches in children, a cochrane review**

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**Background:** Around 10% of children aged 6 to 20 suffer from migraine, losing 1.5 weeks more schooling annually than their peers. Prophylactic drugs can be prescribed when children suffer from frequent/disabling migraine headaches.

**Objective:** To assess evidence from controlled trials on efficacy and tolerability of drugs taken regularly to prevent occurrence and/or reduce intensity of migraine attacks in children.

**Methods:** The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE were searched from 1966 to May 2009 together with articles and books related to headache and prospective randomised-controlled-trials of self/parent administered drug treatments in under-18s with diagnosed migraine.

Headache frequency was the primary outcome measure. Intensity, duration, amount of symptomatic treatment and headache indices were secondary outcomes measures.

Data were extracted from parallel-group and cross-over trials, calculating standardised-mean-differences and odds-ratios from continuous and dichotomous data respectively. Numbers-needed-to-treat and -to-harm were calculated.

**Results:** Placebo-controlled studies for propranolol (a two-thirds reduction (NNT = 1.5, 95% confidence interval (CI) 1.15 to 2.1)) and flunarizine (a SMD of 1.51 (95% CI -2.21 to -0.82)) showed benefits in headache frequency which were statistically significant in favour of flunarizine (p < 0.001). Two placebo-controlled studies on topiramate showed >50% reduction in migraine days/month (OR 1.95, 95% CI 1.06 to 3.95).

**Conclusions:** Propranolol, flunarizine and topiramate showed efficacy for prophylaxis of paediatric migraine.

Conclusive evidence of ‘no effect’ was absent for many drugs, due to small studies with unplanned sample size.

Methodologically sound RCTs for use of prophylactic drugs in paediatric migraine are urgently needed.
IN VIVO characterisation of the prostacyclin receptor in the rat cranio-vascular system

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Background and aims: Prostacyclin (PGI2) induces headaches in healthy volunteers and migraine-like attacks in migraineurs. Increased ictal levels of a PGI2 product was found in jugular venous blood of migraineurs, thus indicating a role for this prostanoid in the migraine pathogenesis. The aim of this study was to investigate the function and expression of the prostacyclin receptor, IP, in rat intracranial arteries.

Methods: Sprague-Dawley rats were used for intravital microscopy on a closed cranial window in vivo. We studied iloprost (a stable PGI2 analogue) (0.01-10 \( \mu \)g kg\(^{-1}\)) induced dilatation of the middle meningeal artery (MMA) and cerebral artery (CA) (n=4-5/group). Furthermore, iloprost (1 \( \mu \)g kg\(^{-1}\) i.c.) induced dilatation was studied in the absence and presence of CAY10441 (IP receptor antagonist) (100-300 \( \mu \)g kg\(^{-1}\) i.c.). PGI2 receptor mRNA and protein expression was investigated in the rat dural and pial arteries by qPCR and Western blotting.

Results: In vivo experiments showed that iloprost dilated rat MMA (\( E_{\text{max}} = 170 \pm 16\% \), \( \text{pED}_{50} = 6.5 \pm 0.2 \)) but not CA. CAY10441 significantly inhibited the iloprost-induced vasodilatory response by 70% in MMA. The expression studies showed that IP receptor mRNA and protein expression was investigated in the rat dural and pial arteries by qPCR and Western blotting.

Conclusion: PGI2 induced dural vasodilatation responses. The response could be inhibited by a specific IP receptor antagonist. This receptor is thus a potential target for the development of anti-migraine drugs.

Alterations of protein expressions during migraine attacks revealed by proteomic analysis

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Background: The activation of the trigeminoafferent system followed by the dilation of the cerebral blood vessels is thought to be the cause of most migraine symptoms. Moreover, the involvement of cortical spreading depression in the emergence of auras is now accepted as an immutable fact. However, the underlying pathophysiology of migraine is still unclear. In this present study, we investigated the alterations of protein expressions induced by migraine attacks using proteomic analysis.

Materials and methods: All patients were carefully interviewed and examined, and diagnosis was made using the ICHD-II. The patient sera were prepared from peripheral blood samples obtained from the 2 migraine with aura patients (MA) and 2 migraine without aura and 3 tension type headache patients. At first, albumin was removed from the patients’ serum samples. Then, we employed them for 2-dimensional gel electrophoresis (2-DE) and 2-DE combined with Matrix-Assisted Laser Desorption/ Ionization-Mass Spectrometry (MALDI-TOFMS). Subsequently, the above data were subjected to database searches for protein identification using a Mascot search engine. Multiple databases such as NCBInr and Swiss-Prot were used in parallel to yield more comprehensive results.

Results: We identified around 10 proteins that significantly differed in expression between pre- and during-migraine periods in each case. Notably, in two MAs, the level of Apo E protein expression during migraine attacks was significantly higher than that before the migraine attacks.

Conclusions: These findings suggest that migraine attacks must affect ApoE expression, which might be relevant to the production of nitric oxide, which is known as a ApoE inducer.

Occipital nerve stimulation with self-anchoring leads for the management of refractory chronic migraine

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Introduction: Occipital nerve stimulators (ONS) has shown efficacy in the management of chronic migraine. However, the incidence of lead migration is significant. In one review it was found to be 60% and 100% one year and three years post-implant respectively. Therefore, we were interested to examine the efficacy and safety of using tined leads for occipital nerve stimulation.
Methods: In this prospective observational study, 12 patients with refractory chronic migraine underwent ONS using a tined lead.

Patients underwent a 7-day percutaneous stimulator trial with a regular Octad lead prior to permanent placement of the self-anchoring lead (tined lead, model 3889) from Medtronic Inc. 

Results: The data were analyzed for 12 patients (10 females and 2 males) with a mean age of 37 (range 25-56). Nine patients had bilateral and three had unilateral lead placement. The mean follow up was 13 months (range 6-18)

Headache frequency (/30 days) improved from a mean of 28 days (baseline) to 16; headache severity (0-10) from 8.2 points to 4.7; HIT-6 scores improved from 72 points to 59; PDI improved from 58.3 to 23.8. One patient had 3-mm lead migration forwards with little change in the stimulation pattern; however without loss of efficacy.

Discussion: The results of this study suggest a role for the self-anchoring lead for ONS in the treatment of medically refractory migraine headaches.

There were significant reductions in headache frequency, severity, HIT-6, and PDI with ONS. None of 12 patients required a surgical revision for lead migration.

PS1-156
Common variation in the SNAP25 gene and migraine predisposition
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Neurotransmitter systems play a pivotal role in common migraine pathophysiology. Recently, an association between STX1A and an increased migraine predisposition was found in a Catalanian and in a Portuguese populations. STX1A encodes Syntaxin 1A, a component of the SNARE complex, involved in the synaptic vesicles’ membrane fusion and subsequent neurotransmitter release.

A case-control association study is being conducted, using the Portuguese sample where association with STX1A was previously assessed, composed of 188 unrelated migraineurs and 287 migraine-free controls, age and ethnically-matched with cases. 19 tagging SNPs of SNAP25 (another member of the SNARE complex) are being studied with total coverage of common genetic variation (MAF>10%) in this gene.

The SNPs’ frequencies in the European population were obtained resorting to the Hapmap, and Haploview v4.1 was used to plot LD patterns and select the tagging SNPs.

The SNPs are being genotyped in multiplex SNaPshot assays. SNaPshot is a powerful, consistent, easy to use, high throughput technique specifically used to genotype SNPs. Results are being analyzed with Genemapper v4.0 software.

Genotyping of all 475 individuals for the 19 SNPs is currently in its final stage, and there are some promising preliminary results.

So far, we have found two significant allelic associations, two significant genotypic associations and a pair of susceptibility haplotypes. Functional consequences for the associated SNPs have been predicted using bioinformatics tools.

Further studies will clarify the role of these genetic variants of SNAP25 in migraine susceptibility, possibly leading to new therapies and pharmacogenomic approaches.

PS1-157
Impact of delaying a triptan during individual migraine attacks
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Background and aims: Triptans reduce migraine pain and associated disability, but delaying triptans reduces their efficacy. To date, a paucity of research has monitored the impact of delaying triptan use during the migraine attack across multiple attacks. The current research evaluated the impact of delaying triptan use on within-attack disability, pain, and associated symptoms.

Methods: A cohort of patients with migraine (n = 207) from a headache center or primary care offices completed 90 days of web-based diaries. The diaries assessed headache characteristics, medication use, and migraine disability (0-10). When triptan use was initiated 60+ minutes after pain onset it was defined as “delayed”. Data was captured within 24 hours (near-time) of the migraine attack. Gamma log-linked GLM was used for the scaled
variables, multinomial GLM for the ordinal variables, and Logit-linked GLM for the binary outcomes. Sequential Bonferroni adjusted 95% CI were used.

**Results:** Among the 2,126 times a triptan was used, 820 times (39%) it was delayed. When a triptan was delayed, disability was significantly greater (M = 5.07 vs 3.76; 95% CID .78-1.84; p < .001), and they had more severe pain (47.3% vs 22.2%; p < .001), nausea (59% vs 49%; CID .01-.20; p < .05), and phonophobia (83% vs 72%; CID .02-.21; p < .01).

**Discussion:** Delaying a triptan increases pain, associated symptoms, and within-attack disability. Patient education about triptan timing is critical.

**Sponsorship:** This study was funded by Merck Sharp & Dohme Corp., Whitehouse Station, NJ, USA and by NIH-NINDS #048288.

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**PS1-158**

**Onabotulinumtoxin a for treatment of chronic migraine: 75% responder analysis results from the double-blind, randomized, placebo-controlled phase of the preempt clinical program**


**Background/objective:** Chronic migraine (CM) is a prevalent and disabling neurological disorder. OnabotulinumtoxinA is the only approved therapy for CM. The results from randomized controlled trials often reflect, but rarely define, the spectrum of subject outcomes. The proportion of subjects highly responsive to a therapy is an important endpoint and guide for clinicians and patients.

**Methods:** PREEMPT (two phase 3 studies: 24-week, double-blind, placebo-controlled, parallel-group phase, followed by 32-week, open-label phase) evaluated onabotulinumtoxinA for prophylaxis of headaches in CM (≥15 days/month with headache lasting 4 hours/day or longer). Subjects were randomized (1:1) to onabotulinumtoxinA (155-195U) or placebo every 12 weeks. The proportions of patients with ≥75% decrease from baseline in frequency of headache days, headache episodes, migraine days, migraine episodes, moderate/severe headache days, and total cumulative hours of headache on headache days were analyzed.

**Results:** Pooled analyses (onabotulinumtoxinA n=688, placebo n=696) demonstrated a statistically significant between-group difference favoring onabotulinumtoxinA in the proportion of patients who had a ≥75% reduction from baseline in headache days at Week 24 (22.8% onabotulinumtoxinA, 15.5% placebo; p=0.002). For all above headache symptom measures, a significantly greater proportion of onabotulinumtoxinA-treated than placebo-treated patients had ≥75% decreases from baseline.

**Conclusions:** PREEMPT supports the efficacy and tolerability of onabotulinumtoxinA for the prophylaxis of headache in adults with CM. These data demonstrate that onabotulinumtoxinA treatment results in a significant 75% reduction in multiple headache symptom measures and highly substantial efficacy for a subpopulation of patients studied.

**Reference:** Dodick DW. Headache 2010;50(6):921-63.

**Support:** Allergan, Inc.

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**PS1-159**

**Field testing chronic migraine (CM) diagnostic criteria: assessment of sensitivity and specificity**


**Background/objectives:** There are several case definitions for CM that differ in the required link to migraine and approach to medication overuse (MO). The Silberstein-Lipton (S-L) criteria are the most inclusive, largely because they use MO as a modifier rather than an exclusionary criterion. Herein, S-L criteria for CM were used as the referent for assessing other criteria for CM in a large database with daily telephonic headache diaries.

**Methods:** For two phase 3 studies (PREEMPT), 2763 CM candidates from 122 centers provided at least 20 days of telephonic diary data prior to randomization. Using S-L criteria as the referent, we calculated the sensitivity (Sn) and specificity (Sp) of 2 alternative definitions of CM. Both definitions require at least half the headache days meet criteria for migraine or probable migraine and identifies forms with and without MO.
Results: Treating S-L CM as the gold standard, the PREEMPT definition had Sn of 75.8% and Sp of 100%. In contrast, the ICHD-2R definition had Sn of 33.2% and Sp of 99.6%.

Conclusions: Using daily telephonic diaries, the PREEMPT definition captures three-fourths of the S-L CM sufferers with perfect specificity. The ICHD-2R definition captures just one-third of the S-L CM sufferers, though specificity remains high. Difference in approach to MO is the major source of diagnostic disagreement.

Supported by: Allergan, Inc.

PS1-160
Field testing chronic migraine (cm) diagnostic criteria: assessments of demographic and headache profiles
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Background/objective: The International Headache Society has tried to establish standardized diagnostic criteria for CM, but it has been difficult, particularly because the causal relationship between medication overuse (MO) and CM is uncertain. The profile concordance between varying CM diagnostic criteria was assessed.

Methods: Two phase 3 studies (PREEMPT) screened 3334 CM patients from 122 centers (6 countries: Canada, US, Croatia, Switzerland, Germany, UK); 2736 had sufficient diary data (≥20 days) and were enrolled into 28-day baseline. Six CM diagnostic criteria variations were analyzed: ICHD-2R=ICHDF-2R (International Classification of Headache Disorders revised); ICHD-2RMO=ICHD-2R with/without MO; S-L-TM=Silberstein & Lipton criteria for transformed migraine (TM); S-L-TMNoMO=Silberstein & Lipton criteria for TM without MO; PREEMPT=diagnostic criteria defined in PREEMPT; PREEMPT-EN=enrolled patients in PREEMPT (met study diagnostic criteria AND all other inclusion/exclusion criteria). Descriptive summary statistics compared demographic/headache characteristics between CM groups.

Results: CM diagnostic groups were similar across demographic profiles and headache characteristics. For all variations, mean age ranged from 38.1 (ICHD-2R/S-L-TMNoMO) to 41.9 (ICHD-2RMO/S-L-TM) years; patients were predominantly Caucasian (range: 84.7% [ICHDF-2R] to 90.1% [PREEMPT-EN]) and female (range: 85.4% [S-L-TM] to 86.4% [PREEMPT-EN]). Frequency of headache days ranged from 18.0 (S-L-TM) to 20.1 (PREEMPT) and frequency of headache episodes ranged from 10.0 (ICHD-2R) to 12.6 (PREEMPT-EN). The percent of patients with MO was 63.6 (PREEMPT), 64.8 (ICHD-2RMO), 64.2 (S-L-TM), and 65.4 (PREEMPT-EN).

Conclusions: Proposed CM diagnostic criteria represent similar patient populations even when stratified by MO. The most controversial issue about CM classification is the role of MO.

Supported by: Allergan, Inc.

PS1-161
Topiromate is effective prophylactic treatment for sporadic hemiplegic migraine
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Objective: To report the case of sporadic hemiplegic migraine (SHM) sufferer who reduced the frequency of SHM attacks using topiromate.

Methods: Case report. Results. A 39 year women presented with 13 years history of SHM (meeting ICHD-2 criteria). 15 years ago the migraine without aura patient with no familial history for hemiplegic migraine experienced mild head trauma. Two years after trauma the patient begun to experience severe headache attacks with a migrainous pattern with 2-4 weeks following episodes of transient sensory loss and hemiparesis in stepwise pattern with frequency 2-4 a year, which resolved without sequelae. During the last year the frequency of such attacks increased until 2/month. The neurological examination during attack revealed left side hemiparesis; CT, ultrasound sonography, cerebral MRI angiography without abnormalities. The EEG showed no evidence of focal discharges. SHM was diagnosed and treatment with Depakine 500mgx2/d started. There were no good results and after 4 months Depakine was changed to topiromate 50mgx2/d. After 2 months of follow up were nearly a 50% reduction of attacks frequency and severity. SHM is defined as migraine attacks associated with motor weakness in the absence of family history. The symptoms of SHM are broadly described but still therapeutic difficulties exist. Based on new pathophysiological insight both migraine and epilepsy are highly comorbid conditions and preventive treatments by new antiepileptic agents seems promising. Conclusion. Prophylactic treatment of topiromate seems to be effective for SHM sufferers particular in cases with frequent attacks.

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Heart rate variability in chronic and frequent migraine patients
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Background and aims: Cardiac autonomic dysfunction in subjects with migraine (episodic migraine, migraine with aura and without) has been already reported, but there are few studies on specificity of cardio-vascular autonomic regulation in chronic migraine (CM). The aim of this study was to investigate the cardiac autonomic function in CM compared with frequent migraine (FM) patients.

Methods: Eighty five patients with migraine, diagnosed according to IHS criteria were enrolled in the study: 57 with CM and 28 with FM (5-14 headache days/month). In all subjects, a 5-min electrocardiographic recording during paced breathing was performed, and heart rate variability (HRV) was analyzed in time and frequency domain according to European Society of Cardiology guidelines.

Results: Low frequency/high frequency ratio representing an index of sympathovagal balance was statistically higher in patients with CM vs. FM (1.50±0.36 vs. 0.63±0.09, p<0.05), a fact suggestive for sympathetic hyperactivity in CM. The activity of suprasegmental centers was considerably higher in CM patients compared with FM with a statistically significant higher value of VLF % index (31.63±5.76 vs. 16.43±3.41, p<0.05) and index of centralization (IC) (3.44 vs. 0.96, p<0.01). SDNN and pNN50% were significantly lower in CM (p<0.05 and p<0.01, respectively), reflecting an over-activation of sympathetic influences on cardiac rhythm.

Conclusions: The peculiarities of autonomic regulation of cardiovascular system in CM as compared with FM are the relative over-activation of sympathetic nervous system, a more pronounced reduction of parasympathetic influences with signs of important intensification of suprasegmental autonomic structures’ activity.

Effectiveness of an aerobe sports programme in migraine

Background and aims: Sport has a positive effect of the quantity, duration and intensity of migraine attacks. Negative increased amplitudes of the contingent negative variation (CNV) in migraine are frequently examined. Up to now it isn’t examined which effects sport has on the CNV (habituation, iCNV and preactivation level). The aim of this study is to investigate the influence of sport on slow cortical potentials (CNV) in migraine patients.

Methods: 16 patients were examined and randomized at two groups. The first group got a ten-week aerobic sports programme three times a week with a trainer. Eight patients without physical training served as a control group. During the whole study the groups filled out a migraine-diary and the iCNV, the habituation and the preactivation level was measured before and after the training.

Results: Patients of the jogging-group showed a significant change of the CNV-parameter habituation (increase of habituation = reduction of dishabituation) (p=.024*).

Conclusions: Sport leads to an increase of habituation velocity. This reduced dishabituation of migraineurs could be interpreted as an improvement of the selective attention. Our interpretation is due to the sport it comes to a noradrenergic regulation what leads to a improved habituation. This improved habituation could be understood as an improvement of a dysfunctional initial information processing and an stimulus selection. The results show that this sports programme improved the inadequate attention selection of the migraine patients. Further studies should proof the noradrenergic processes after sport by migraine patients.
Background and aims: Sport has a positive effect of the quantity, duration and intensity of migraine attacks. Up to now a few studies had proved this effect. But the direction of this effect isn’t clear yet. The aim of this study is to examine the influence and the direction of the effect from sport of headache-parameter of migraine.

Methods: 16 patients were examined and randomized at two groups. The first group got a ten-week aerobic sports programme three times a week with a trainer. Eight patients without physical training served as a control group. During the whole study the groups filled out a migraine-diary and also questionnaires about complains (BL, BDI) and stress-coping (SVF) before an after the training.

Results: Patients of the jogging-group showed a reduction in the number of migraine days (p = .048) and in the intensity of the attacks (p = .028) per month. Stress strategies like “displacement activity” (r = -.715; p = .046), “looking for self-confirmation” (r = -.742; p = .035) and “feelings of aggression” (r = -.802; p = .017) were reduced. Increasing the level of fitness is one predictor for migraine improvement (r = .409).

Conclusions: Sport which leads to a better fitness-level is an alternative therapy method in migraine. This pilot study shows the positive effect of a ten-week aerobic sport three times a week on the quantity and intensity of migraine attacks. Moreover, the running exercise decreases stress signs like aggression, displacement activity and looking for self-confirmation. The increase in the level of fitness is one predictor for the migraine improvement.

PS1-165
Greater occipital nerve block for medication overuse headache

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Background and aims: Local anesthetic or steroid injection to great occipital nerve could be an alternative treatment for such resisting patients. The study aims to evaluate the local anesthetic injection to great occipital nerve and the response to the pain in the period when the symptoms of discontinuation emerges after ending the overused medicines in the course of treatment of medication overuse headache (MOH).

Methods: A total of 38 patients, aged 18-65, migraine without aura in their anamnesis, meeting the MOH diagnosis criteria and who have accepted greater occipital nerve (GON) block treatment. The efficacy of the GON block were made by visual analogue scale (VAS) and by calculating the monthly total pain index (TPI). The patients were applied 1ml-%1 prilocain in the first injection for diagnosis purposes, and 1ml-%0.5 bupivakain during the second and third injections, and three GON blocks with a week break amongst each.

Results: In the application of GON block made for diagnosis purposes, the difference between the VAS value before the injection and the one calculated at the 15th minute was statistically significant (p < 0.05). The difference between the VAS value before the injection and the one after the 3rd injection was statistically significant (p = 0.000). The difference between the TAI value before the injection and the one in the 1st month after GON block were found statistically significant (p < 0.001).

Conclusions: Our results indicated that the GON block is effective in the process of MOH detoxification.

PS1-166
Temperament and character profiles of patients with tension-type headache and migraine

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The aim of this present study was to evaluate the temperament and character profiles of persons with tension-type headache (TTH) and migraine, and to compare the results with of two. The study population consisted of 42 patients with TTH (35 female, 7 male) and 11 patients with migraine (1 female, 10 male) aged 18-50 years, according to the criteria of the International Headache Society with age and gender.

All participants were instructed to complete a self-administered 240-item temperament, edinburgh hand dominance and character inventory (TCI) questionnaire and Beck Depression Inventory (BDI).

The TCI assesses four dimensions of temperament, namely, novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence (P) and three dimensions of character, being self-directedness (SD), cooperativeness (C) and self-trascendence (ST).

It was found that mean BDI scores were higher (not significant) in patients with migraine (14.7) than TTH (8.5).
No significant differences were found between the groups regarding main NS, RD, PHA, SD, C and ST scores. SD scores is lower in migraine also ST scores is lower in TTH. The main result of this study is migraine patients are relatively more prone to depression than TTH.

PS1-167

The prevalence of chronic and episodic migraine in children and adolescents

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Migraine is the most important cause of the headache related decreased quality of life in children and adolescents. The prevalence of episodic (EM) and chronic migraine (CM) increase with age, especially in the last years of adolescence.

In order to evaluate the prevalence and variables of migraine in children and adolescents with “episodic or chronic” migraine we performed a school-based epidemiological study. First part of the study was conducted in 2001 in 5562 schoolchildren. Second part of the follow-up study was performed in 2007 in 1155 adolescents. Following the publication of these epidemiological reports, a new retrospective analysis of our database was made regarding migraine and its features.

10.4% of the children were diagnosed with migraine, of whom 1.7% had CM and 3.8% had EM, with a higher tendency in advancing age and in girls. Frequency of CM increased with age, doubling at age 12 (p=0.035). All of the subjects with EM showed a higher frequency of positive family history for headache than CM. CM sufferers reported longer headache duration, generalised pain location, early morning onset attacks and aggravation by physical activity compared to EM (p<0.05).

In adolescents, 18.6% were diagnosed with migraine. 1.5% had CM, 4.8% had preCM and 3.8% had LwFrEM. The frequency of PreCM increased with age. The binary logistic regression analysis showed that age, gender and a positive family history of headache for both of father and siblings was correlated with migraine chronification (p<0.05).

In children, 10.4% were diagnosed with migraine of whom 1.7% had CM, 4.8% had preCM and 3.8% had LwFrEM. The frequency of PreCM increased with age. The binary logistic regression analysis showed that age, gender and a positive family history of headache for both of father and siblings was correlated with migraine chronification (p<0.05).

In adolescents, 18.6% were diagnosed with migraine. 1.5% had CM, 4.8% had preCM, and 2.7% had LwFrEM with all showing a high frequency in girls and at youger. PreCM sufferers showed an intermediate effect for headache severity, pulsating quality, aggravation by physical activities, having any associated feature and unilateral location between CM and EM sufferers.

Our results suggest that preCM may be a transitory medical condition and as considered a prechronic state it should be evaluated comprehensively, in order to be diagnosed and to prevent its evolution into CM at the earliest possible time. We also propose the addition of the term preCM to increase awareness this condition.

PS1-168

Is there a prechronic stage of chronic migraine in children and adolescents?

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One of the current questions is whether and how many of the children and adolescents with episodic migraine (EM) are prone to develop CM?

In order to answer this question we evaluated the prevalence and clinical variables of patients with migraine. CM-group (≥15 migraine days/month), the EM-group (subclassified as the “low frequency EM” (LwFrEM), ≤10 migraine days/month), and preCM (between 11-14 migraine days/month) have been defined. We restudied our school-based epidemiological studies published before (First, in 2001 in 5562 and 2nd, in 2007 in 1155 persons).

In children, 10.4% were diagnosed with migraine of whom 1.7% had CM, 4.8% had preCM and 3.8% had LwFrEM. The frequency of PreCM increased with age. The binary logistic regression analysis showed that age, gender and a positive family history of headache for both of father and siblings was correlated with migraine chronification (p<0.05).

In adolescents, 18.6% were diagnosed with migraine. 1.5% had CM, 4.8% had preCM, and 2.7% had LwFrEM with all showing a high frequency in girls and at younger. PreCM sufferers showed an intermediate effect for headache severity, pulsating quality, aggravation by physical activities, having any associated feature and unilateral location between EM and CM sufferers.

Our results suggest that preCM may be a transitory medical condition and as considered a prechronic state it should be evaluated comprehensively, in order to be diagnosed and to prevent its evolution into CM at the earliest possible time. We also propose the addition of the term preCM to increase awareness this condition.

PS1-169

The effect of NMDA antagonist on nociceptive response of trigeminocervical complex in facial formalin model

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Background and aims: NMDA receptors are known to be involved in transmission of nociception in central nervous system. Activation of trigeminal afferents innervating sensory dermatome of ophthalmic branch result in neuronal activation in the trigeminocervical complex (TCC). This study was aimed to investigate the influence of NMDA receptor antagonist, memantine on pain pathway in the trigeminocervical complexes using formalin induced facial pain model.

Methods: In Spargue Dawley rat, formalin or vehicle was delivered in form of s.c injection into the left upper eyelid (V1 branch). Memantine (10mg/kg) or vehicle was injected intraperitoneally 30 minutes before formalin test. The sensory threshold for mechanical stimulation (von Fray filament) (PWML) were measured before and 2 hours after formalin injection. The nociceptive behaviour was measured by monitoring the time spent for rubbing of the injected area with the ipsilateral forepaw during 60 min after formalin injection. The rat underwent intracardiac perfusion, and the brain, including the brainstem, was removed. Following fixation, sections that spanned the TCC were cut, reacted with a Fos antibody and visualized using ABC amplification system.

Results: Pretreatment of memantine significantly attenuated formalin induced nociceptive behavior (P < 0.05). The sensory threshold checked with PWML test did not change after memantine pretreatment. In the TCC, the number of Fos-positive cells increased following formalin injection. The increment of formalin induced Fos-immunoreactivity was significantly attenuated in pretreatment of memantine compared to control (P < 0.05).

Conclusions: The present study suggests that NMDA receptor anagonist, memantine might inhibit in facial sensory nociceptive transmission to TCC.

PS1-170
Clinical trial design in chronic migraine: lessons learned from the ninds crc chronic migraine treatment trial (cmtt)
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Objective: Design an efficient randomized placebo-controlled clinical trial of combination therapy in chronic migraine.

Background: Open-label studies and conventional wisdom suggest the combination of two migraine preventive agents may result in incremental benefit over a single agent. Prior to CMTT, no randomized trials had assessed the value of frequently used preventive agent combinations for chronic migraine (CM). CMTT was expected to randomize 250 CM subjects not adequately controlled (≥10 headaches/month) with topiramate (50mg/day-100mg/day) to either the addition of propranolol LA (up to 240mg/day) or placebo.

Design/methods: International Classification of Headache Disorders-II (ICHD-II) guidelines and diagnostic criteria were used. Initial eligibility required subjects with CM already on preventive medication to undergo a two-month washout period. Current stable topiramate use (50-100/mg/day) was permitted. Subjects not taking topiramate were required to complete a 4-week topiramate titration-phase prior to 28-day baseline diary completion.

Results: 70 sites were activated and 48 randomized at least one subject. Unwillingness to terminate other migraine preventatives for two months contributed to subject screening ineligibility. 68% initiating screening failed to randomize. Primary reasons for randomization failures were loss/refusal of follow-up (30%), too few headaches (23%), and inability to tolerate ≥50mg/day topiramate (19%). The number of headaches required for eligibility after topiramate titration was modified from 15 to 10 days/month to minimize ineligibility rates and increase the number of subjects who could be randomized.

Conclusions: Lessons learned from CMTT regarding trial design, implementation, and recruitment, will inform the design of future trials evaluating the efficacy of combination preventive medications in CM subjects.

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PS1-171
The analgesic effect of alcoholic extract of tanacetum parthenium on pain in mice in formalin model
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Background and aims: Medicinal herb are very useful in Shahrekord, Iran

Methods: Analgesic effect of Tanacetum parthenium was evaluated by formalin test in mice. Different doses of Tanacetum parthenium ethanolic extract and the positive and negative control groups and naloxone groups comprised the study. 15 minutes before formalin injection in foot floor of mice, different doses of extract, ibuprofen, morphine and naloxone injected intraperitoneally in mice. In this experiment 100 mice were divided into 10 groups as follows: group normal salin, groups received 10, 20, 30, 40 and 80mg/kg of alcoholic extract, respectively. Group received 100 mg/ kg ibuprofen, Group received 0.5 mg/kg morphine, respectively, group received 0.5 mg/kg naloxon and group received naloxon and extract. The data were analyzed with SPSS software version 17 using Kruskal wallis and Dunn post hoc test.

Results: Among the different doses of extract, 10mg / kg has more analgesic effect and showed significant difference with groups ibuprofen and distilled water (p < 0.05). The results indicates that the analgesic effect of Tanacetum parthenium is dose dependent and it is significant at 10 mg/kg (p < 0.05). The analgesic effect of the extract was inhibited by naloxon.

Conclusion: Tanacetum parthenium contains flavonoids and its antinociception action should be, at least in part, due to inhibition of prostaglandine synthesis.

Material and methods: The study included two groups with 93 patients with CM and 441 patients with EM. The diagnosis was established accordingly to International Classification of Headache Disorders, 2nd edition (ICHD II) criteria. All patients were interviewed with a detailed structured questionnaire regarding the following migraine comorbidities: pain in different body parts, generalized anxiety and panic attacks, depression and sleep disturbances.

Results: CM patients had a statistically significant higher frequency of pain of different location as compared with EM, more often being seen chest pain, abdominal pain and limb pain (p < 0.05). Generalized anxiety (7.5 % vs. 3.6 %, p < 0.01) and panic attacks (44.4% vs. 24.9%, p < 0.001) were more frequent in CM group as compared with EM. Other important differences between the groups were in the depressive symptoms (like reduced/increased weight, reduced appetite, sleep problems, sense of guilt and suicidal thoughts, p < 0.05) and sleep disturbances (with increased daytime sleepiness, 74.4 vs. 65.5 %, p < 0.05), all of them being more common in CM (p < 0.05).

Conclusions: Anxiety, depression, sleep disturbances and other pain symptoms are the most common comorbidity disorders in chronic migraine. Systematic evaluation of comorbidities should be an important part in the clinical examination of a migraine patient, since some of them could lead to headache chronicization.

PS1-173

MRI studies in patients experiencing migraine with perpetual aura

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Introduction: Migraine with perpetual or persistent aura is effectively untreatable. Previous studies of typical transient migrainous aura reported marked hypoperfusion. One published series of four patients with persistent aura found no changes in water diffusion or brain perfusion in dynamic susceptibility MRI.

Subjects & methods: Data were acquired from five patients with migraine with perpetual visual aura and eight healthy volunteers of similar ages using a Siemens 3T Verio MRI system. Tissue water apparent diffusion coefficient (ADC) and relative CBF (rCBF) were calculated from manually selected regions of interest. rCBF measurements from visual cortex were normalised to the mean frontal/parietal values. Resting state fMRI data was analysed using FSL software.

PS1-172

Frequent comorbidities in chronic and episodic migraine: data from the epidemiological study in the republic of moldova

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Background: Comorbid disorders are important factors in progression and clinical evolution of primary headaches as chronic migraine (CM).

The aim of the study was to determine the differences in comorbidities in chronic and episodic migraine (EM).

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Results: Visual inspection identified no focal abnormalities of water diffusion or perfusion in any of the subjects. ROI analysis revealed no significant differences in ADC or corrected rCBF between any individual subjects or the migraine group compared to normal control subjects. Resting state fMRI networks differed between controls and migraine subjects, although with variable patterns.

Discussion: These perfusion and DWI results accord with the only previous published study in this subject group, which used different methodology for perfusion measurement. Results so far suggest that perpetual visual aura is not associated with demonstrable brain perfusion or apparent isotropic ADC abnormalities. This contrasts with perfusion changes associated with typical migraine aura and headache. Differences in ‘resting state’ activity revealed by BOLD fMRI, which is highly sensitive to regional brain networks through vasoreactive coupling, suggest a potential imaging biomarker of persistent migrainous aura.

PSI-174
Effects of repetitive transcranial magnetic stimulation in chronic migraine: a pilot study
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Background: Improvements in frequency and severity of migraine attacks were reported in a patient with depression, treated with active transcranial magnetic stimulation of the left dorsolateral prefrontal cortex (rTMS-DLPFC). We performed a pilot double-blind, randomized clinical trial to compare effects of active and placebo rTMS-DLPFC in patients with chronic migraine.

Methods: Thirteen women diagnosed with chronic migraine were randomized to either active (n=7) or placebo (n=6) sessions of 10Hz rTMS-DLPFC over eight weeks (total, 23 sessions; 1600 pulses per session). The primary endpoint was the percentage of responders (showing at least 50% decrease in the number of pain days). Secondary outcomes were: number of pain days and pain severity in the past month. Outcomes were evaluated at baseline, after 1 and 2 months of treatment.

Results: One patient in the active group and one patient in the placebo group dropped out after the first week of treatment. In intent-to-treat analysis, 1/7 (14.3%) patients in the active and 1/6 (16.7%) in the placebo groups responded to 1 month of treatment. At 2 months, 3/6 (50%) of patients in the placebo group, and none of the patients in the active group responded. The number of days with pain decreased significantly in patients in the placebo group, and pain severity decreased significantly in patients in the active group after 2 months, but not after 1 month of treatment.

Conclusions: The results of this pilot study indicate strong placebo effects of rTMS-DLPFC in chronic migraine, that deserve further investigation in a larger trial.

PSI-175
Activation of tyrosine metabolism in chronic migraine: pathogenic relevance
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Several lines of evidence show that migraine without aura sufferers are characterized by an anomalous tyrosine metabolism profile with non-physiological levels of catecholamines: high dopamine (DA) and low noradrenaline (NE) levels in plasma along with high levels of elusive amines (i.e. octopamine and synephrine). Very little is known about plasma catecholamines levels in chronic migraine, therefore we evaluated the plasma levels of DA and NE in a group of 16 control (10F, 6M, age 27-49 years, mean 34.0) and 19 chronic migraine sufferers (14F, 5M, age 18-64, mean 46.7). The diagnosis was made in agreement with IHS criteria II eds. In each patients the frequency of migraine attacks was at least 20/month and all patients suffered from headaches for at least 25 days/month. All patients assumed acute treatment for migraine attack almost daily. The DA and NE plasma levels were performed utilizing coulimetric HPLC.

The levels of DA and NE were significantly higher in plasma of the chronic migraine sufferers in comparison to those of normal control subjects (p<0.05, p<0.01 respectively). These findings not only support the hypothesis that an anomalous tyrosine metabolism characterizes chronic migraine leading to an increase of catecholamines in plasma, but also confirm that anomalies in DA synthetic pathways play a role in the pathogenesis of migraine without aura. The increased levels of NE in chronic patients, in contrast to those found in episodic migraine, suggest that noradrenergic system may play a role in the transformation of episodic to chronic migraine.
PS1-176
Quantitative assessment of blood-brain-barrier permeability in a mouse model of migraine by dce-mri
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Background: Patlak plot analysis of dynamic contrast-enhanced magnetic resonance (DCE-MRI) images enables the quantification of blood-brain barrier (BBB) leakage following various cerebral traumas. Typically contrast agents are administered via the tail vein, which, when repeated, cause scarring; the insertion of permanent canulae requires an invasive procedure and is prone to infection and damage by grooming.

Aim: We developed a method for quantification of longitudinal DCE-MRI using intraperitoneal administration of an MRI contrast agent (CA) and tested this protocol to assess BBB changes after cortical spreading depression (CSD) in transgenic mice with a pathogenic familial hemiplegic migraine type 1 (FHM1) gene mutation.

Methods: CSD induction was performed by topical 1M KCl application to the occipital cortex of the right hemisphere of heterozygote mutant mice bearing the FHM1 S218L mutation. In vivo T1W RARE MRI brain scans were taken with a Bruker 9.4 T system. The changes in permeability of the BBB were assessed by Patlak plots without arterial input function (AIF), by employing the temporal muscle as reference region.

Results: BBB leakage was estimated using ROIs for the entire cortex in both hemispheres. The Patlak plots showed linearity up to 72 minutes post intraperitoneal injection of CA, demonstrating that the CA was transferred unidirectionally from blood to brain, and that the transfer was not limited by the blood flow but by the BBB.

Conclusion: BBB permeability can be calculated with confidence following intra-peritoneal administration of MRI CA, in a longitudinal setup.

PS1-177
Case-control candidate-gene association study in spanish migraineurs
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Background and aims: Endothelin B receptor (coded by EDNRB) regulates vasoconstriction. EDNRB rs2329047 polymorphism has been associated with migraine with aura (MA) females due to the minor homozygous genotype. Increased gene expression levels of Alpha-fodrin, a spectrin family protein (coded by SPTAN1), have been associated with migraine.

A candidate-gene association study was done to determine if Single Nucleotide Polymorphisms (SNPs) of these genes are related to migraine, in a Spanish population.

Methods: We genotyped 4 tagSNPs of EDNRB (rs2329047 and rs18017808) (from previous studies) and SPTAN1 (rs10819406 and rs13299607) (from Hapmap data, r2 > 0.8, CEU population and tagger pairwise selection) in a cohort of 961 migraineurs and 801 non-migraineurs recruited in a Headache Unit. DNA was extracted with Chemagen® extraction kit and/or salting-out method; the SNPs were genotyped with Veracode GoldenGate technology (Illumina). Statistical analysis was performed using Chi-square and Fisher exact test in SPSS v15.

Results: 956 cases and 793 controls were successfully genotyped for rs2329047. GG genotype was associated with migraine under a dominant inheritance model [cases 58.7%; controls 41.3%; p=0.011] and also the G allele in the additive model [cases: 56%; controls 44%; p=0.049].961 cases and 801 controls were successfully genotyped for rs13299607. GG genotype was associated with migraine under a dominant inheritance model [cases 56.2%; controls 43.8%; p< 0.045].

A significant association of rs180170 or rs10819406 was not observed with migraine.

Conclusions: Rs2329047 and rs13299607 are associated with migraine in a Spanish population. Functional studies are needed to investigate the contribution of these genes to migraine pathophysiology.

PS1-178
Clinical characteristics associated with the chronification of migraine: the chromig study
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**Background and aims:** Migraine attacks can increase in frequency over time. Patients can be classified as suffering from episodic (EM) or chronic migraine (CM).

We present a descriptive analysis of clinical characteristics of migraineurs in a Spanish population, with interest in factors associated with chronification.

**Methods:** Patients were recruited in a Headache Unit. The following data was analyzed: sociodemographics, comorbid disorders, attacks and treatments. Patients completed the HIT-6, MIDAS, STAI, BDI and SF-36v2 scales. The characteristics between EM and CM were compared.

**Results:** 1109 patients, 879 (79.3%) EM and 230 (20.7%) CM, were recruited following ICHD-II criteria. The univariate analysis of the characteristics associated to chronification showed that lower education, vertigo, childhood symptoms, chronic fatigue syndrome, allodynia (p < 0.05); and sleep disorders, psychiatric familiar history, lower mass corporal index, anxiety-depressive syndrome, as well as, excessive acute medication use, greater triptan and preventative treatment use together with a greater disability in all disease impact scales (p < 0.001) were linked to CM.

A logistic regression model found three risk factors for CM associated in an independent manner: abuse of medication [OR = 3.84; IC (2.18-6.75); p < 0.001], disability on MIDAS scale (severe) [OR = 1.36; IC (1.16-1.60); p < 0.05] and on the STAI-E (state anxiety) scales [OR = 1.27; IC (1.02-1.58); p < 0.05].

**Conclusions:** The clinical characteristics associated with CM in this study are similar to other studies. Only the use of excessive acute medication, a greater disability on the MIDAS scale and the presence of state anxiety (STAI scale) are risk factors associated in an independent manner with CM.

**PSI-179**

**Headache culture in italian people: where are we?**


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**Introduction:** Every year the Italian Society for the Study of Headache (SISC) celebrates the National Headache Day and organizes educational programs with the aim of spreading headache culture. In the occasion of the second anniversary, on May 20 2009, a survey was conducted to obtain information concerning people perception of headache.

**Methods:** A gazebo was set up in the main squares of six Italian cities: Bari, Catania, Rome, Padova, Pavia and Perugia, and a questionnaire on headache was proposed to bystanders. Data were collected in a spreadsheet and analyzed.

**Results:** The questionnaire was filled up by 449 subjects and 332 of them declared to suffer from headache. Among headache sufferers, 19.28% revealed to have never heard before about any Headache Centre. Headache resulted to be managed by a General Practitioner in 28.09%, by a Specialist in 17.81%, by a Headache Centre in 30.55% and by the patient himself in 23.64% of the cases. About 11% of patients had referred to Emergency Room one or more times in the previous year. Headache was perceived as a hard or very hard worry by 67.38% of them. Only 34.27% revealed to take specific headache therapies. The most impressive definitions of headache were: “a time bomb”, “a trap”, “an enemy”, “a curse”, “a nightmare”, “a fog”, “a persecution”, “a bother”.

**Discussion:** Although not having an epidemiologic value, these results stress the need for further educational programs involving the general population to spread headache culture and optimize the access to health care resources.
PSI-180
Effects on habituation of preventive migraine therapy with topiramate: a laser evoked potential study
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Background: It has been hypothesized that some preventive treatments might protect migraineurs brain from attacks by stabilizing cortical excitation level and thus the response to external nociceptive stimuli.

Aim of this study was to investigate the effects of preventive treatment with topiramate on cortical responses to nociceptive stimuli induced by Laser (LEPs) in migraine patients.

Methods: Scalp potentials were evoked by Nd-YAP Laser stimulation of the hand and first trigeminal division in 13 patients with migraine without aura (MO) and 14 control subjects (CS). The exam was repeated twice in MO patients, before (T0) and after (T1) two month treatment.

Results: Topiramate was effective in all MO patients in reducing intensity and frequency of attacks, and we confirmed the lack of habituation typical of MO patients (p=0.05). Moreover, treatment was significant in normalizing the habituation pattern in MO patients for the N1 component, generated in the secondary somatosensory cortex (SII) (p=0.05), but not for the N2/P2 complex, generated in the anterior cingulated cortex (ACC). We also observed a significant correlation between clinical effects and normalization of neurophysiological responses (p=0.001, r=0.838).

Conclusions: Our results indicate a modulating action of topiramate on cortical processing of sensorial stimuli, regarding the sensory-discriminative component of pain, elaborated by the SII, without a significant effect on the affective dimension of pain, in which the ACC has an important role. We therefore demonstrate that the significant improvement of symptoms in MO patients can be related to the effects of topiramate on modulating cortical responses in the SII.

PSI-181
Simulation of gtn provoked migraine in an awake animal model

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Background and aims: GTN (an NO donor) has a short half life and the headache induced in migraineurs after GTN infusion is most probably a result of activation of certain cascades which still are not known. The aim of the present study was to simulate human GTN provoked migraine in awake rats and investigate the mechanism behind these induced headaches.

Methods: The animal model was developed by infusing GTN in a dose 4μg/kg/min, for 20 min, i.v. in awake rats. The mRNA and protein expression for c-fos, nNOS and CGRP were analysed in the trigeminal vascular system at different time points after the GTN infusion using RT-PCR, immunohistochemistry, Western blotting and CGRP release studies.

Results: GTN infusion did not induce hypotension in awake rats in contrast to anaesthetized rats. Significant upregulation of nNOS mRNA in dura after 30 mins was followed by an upregulation of nNOS protein at 4 hrs after GTN infusion. Upregulation of c-fos protein in TNC at 2 and 4hrs after the infusion was observed. The activation at 4 hrs was inhibited with the pre-treatment of L-NAME or sumatriptan by 60% and 50% respectively. In addition, increase in CGRP expression was observed at 2 and 4hrs in TNC and at 4 hrs in dura along with 45% increase in CGRP release in dura.

Conclusion: Increased NO tone as a direct result of GTN infusion and/or due to upregulation of nNOS in concert with enhanced CGRP release may be the key events in migraine provocation after GTN infusion.

PSI-182
Innovative, on-line, searchable data base for headache
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Objective: To develop a web-based headache history and diagnostic tool to collect and organize large data sets.

Background: Large data bases of headache signs and symptoms have been generated primarily via manual input in a doctor's office, computer generated phone calls followed by semi-structured interviews and
retrospective chart reviews. Larger comprehensive public-licy-generated data bases do not exist. We developed a computer-based program that allows patients to enter a detailed history in a deidentified manner on the web and a rule-based diagnostic engine based on ICHD-2 criteria.

Methods: An interactive headache history, developed by headache experts, provided input for a propositional rule-based classification tool developed by a computer expert in Java and deployed using Google Web Toolkit and PHP. The instrument was placed on a private website and six headache specialists invited six new patients each to enter their headache histories. Between 56 and 347 data points were entered by each patient. The output was expert narrative reports and diagnostic impressions. Subsets of data were collected to validate the instrument and assess its usability and versatility. The data is stored in a SQL database and can be used to re-generate different views of the patient history and diagnosis on the web, allowing remote viewing when local experts are scarce while preserving privacy. The diagnostic rules allow for simple explanations of findings. They can also be used to highlight small changes in the history that would lead to a different diagnosis, indicating aspects most likely to require the attention of a physician.

Results: 25 patients completed the questionnaire. Migraine without aura, migraine with aura and cluster were all accurately diagnosed. There were no other primary headaches identified. Subsets of data supporting or refuting the diagnosis and red flags suggesting secondary headache were easily extractable.

Conclusion: This preliminary study demonstrates that an internet computer-based program can collect and organize a large set of variables from a headache history. Multiple applications are possible in clinical medicine and research.

PSI-183
Implementation of invasive procedures in the treatment of patients with chronic facial pain or headache syndromes
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Background: Usually the treatment of chronic facial pain (CFP) or chronic headache syndromes (CHS) is conserva-tive, pharmacologically and psychologically and conducted in specialized centres. A certain percentage of these patients remain refractory to any treatment or suffer from intolerable analgesics side effects. Invasive procedures should be discussed for these selected patient groups.

Methods: Peripheral subcutaneous nerve stimulation (PNS) of the trigeminal nerve branches or the greater occipital nerves (ONS) is performed for patients with CFP or CHS. Also epidural cervical dorsal column stimulation (SCS) is performed for CHS. Deep brain stimulation (DBS) of the medial thalamus or posterior hypothalamus is used in CFP or CHS. Epidural cortical stimulation (MCS) of the facial motor strip is performed in CFP.

Results: Whereas PNS, ONS and SCS are suprathreshold stimulations with evoked paraesthesias a pain reduction but no pain free status could be evaluated. Additionally complication rate was very low. DBS and MCS are sub-threshold giving the advantage of double-blinded testing and identification of false-positive responders. In case of pain reduction of more than 30%, accompanied by reduction of analgesics and increase of quality of life, implantation of a neurostimulator was performed.

Conclusion: For selected patients with CFP and CHS invasive procedures like PNS, ONS, SCS, DBS and MCS should be implemented to the multimodal and interdisci-plinary treatment setting. Patients should be advised to experienced centres for functional neurosurgery and special-neurosurgical invasive pain treatment. Therefore the interdisciplinary cooperation between conservative and invasive pain specialists needs to be advanced and improved.

PSI-184
Combined occipital and supraorbital neurostimulation for chronic migraine headaches: an extended case series
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Introduction: In 1999 we introduced occipital nerve stimulation (ONS) as a novel treatment for occipital neuralgia. Subsequent investigators extended the methodology to migraine headaches with the results suggesting a lower response rate than that for occipital head pain. Hypothesizing that the addition of supraorbital stimulation may improve the results for migraines, we developed the associated procedure and in 2010 reported positive results in a series of 7 patients treated by combined occipital nerve-supraorbital nerve stimulation (ON-SONS). Thereafter, we further perfected the protocol and
between 2004 and 2010 implanted the system in 93 patients with chronic migraine headaches.

**Methods:** A retrospective survey was offered to 93 patients who had combined ON-SONS systems implanted. Included were scores for the Short Form-12 (SF-12), Migraine Disability Assessment (MIDAS), headache frequency and severity, med usage, patient satisfaction, and patient preference for either the combined or single modality therapy (ON-SONS vs. ONS).

**Results:** 44 patients responded. All results were significant to $p < .05$. The average time since implant was 13 mo. The frequency of severe headaches per month decreased by 81% (19 to 3.6/mo), and 50% of respondents saw virtually complete resolution of headaches (0-1/mo). 73% of patients decreased med usage by over 75%. The SF-12 score improved by 61% and the MIDAS by 84% (170.8 to 26.7). 87% were pleased, and all preferred combined ON-SONS to ONS alone.

**Conclusion:** Combined ON-SONS provides effective therapy for some patients with chronic migraine headaches. The therapeutic response appears to be markedly superior to ONS alone in most patients.

**PSI-185**

**Involvement of pain and reward systems in medication-overuse headache**

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Medication-overuse headache (MOH), a significant medical problem, most frequently evolves from episodic migraine, the mechanisms remaining unclear. Patients with MOH frequently fulfill diagnostic criteria of substance dependence and are comorbid with other substance related disorders. Thus neurobiological similarities between MOH and substance dependence have been suggested. Using voxel-based morphometry, we searched for structural abnormalities related to pain and reward.

High-resolution structural MRIs were compared between 29 patients with both, MOH and migraine, according to IHS diagnostic criteria and healthy age- and sex-matched controls. Comorbid anxiety and depression were assessed with the HADS.

In patients, we observed a significant increase of grey matter volume (GMV) bilaterally in the thalamus, the ventral striatum, the hippocampus, the middle cingulum, the inferior cerebellum, and the periaqueductal grey matter of the midbrain. We found a significant GMV decrease in prefrontal regions, the left insula, and the left temporal pole. Ten patients with HADS-scores $< 8$ on each subscale showed only a GMV decrease in the right insula, and in the anterior cingulate cortex. Patients and controls had distinct patterns of grey matter covariance in pain processing and modulatory regions, suggesting altered functional connectivity.

In patients with MOH, we found structural changes in pain processing regions including the brainstem. Furthermore, we found grey matter changes in fronto-striatal systems. This is compatible with the concept of dependence as a disease maintaining factor in a subgroup of patients with MOH. Further, MOH patients with low HADS scores had less pronounced structural changes without involvement of reward systems.

**PSI-186**

Migraine associates with molecular markers of endothelial dysfunction

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**Background and aims:** Interest in relation between endothelium and migraine has increased in recent years. Our aim is to determine the presence of endothelial dysfunction in migraine not only during the interictal period but also during migraine attacks, studying molecules involved in migraine physiopathology and endothelium.

**Methods:** Prospective study of 47 migraineurs (33 migraines without aura and 14 migraines with aura) and 23 control subjects, without known vascular risk factors and free of acute or chronic inflammatory/infectious conditions. Diagnosis of migraine was established by IHS 2004 criteria. We determined molecular markers during migraine attacks and in the interictal period and compared it with the values in healthy control subjects. Molecules quantified were stable metabolites of nitric oxide (NOx), calcitonin gene-related peptide (CGRP) and vascular endothelial growth factor (VEGF).

**Results:** Higher levels of NOx ($1225.2 \pm 466.1$ vs $671.9 \pm 358.6$ mM; $p < 0.0001$), CGRP ($164.2 \pm 139.1$ vs $37.1 \pm 38.5$ mg/ml; $p < 0.0001$) and VEGF ($473.4 \pm 398.7$ vs $72.6$...
± 56.6 pg/ml; p < 0.0001) were found in migraineurs in a basal period, in comparison with healthy controls. An increase in NOx (1656.8 ± 259.5 mM; p < 0.0001) and CGRP (298.2 ± 100.3 mg/ml vs; p < 0.0001) was observed during headache. VEGF values (457.8 ± 271.5 pg/ml; p = 0.359) did not reach statistically significant differences during migraine.

**Conclusions:** In our study endothelial function measured by molecular markers was found altered in patients with migraine in the interictal period and during acute headache.

**PSI-187**

**Migraine and endothelial function: relation between ictal and interictal period**

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**Background and aims:** Recent investigations in migraine physiopathology have focused in its relation with endothelium with different results. We aim to study endothelial function with molecular and ultrasonographic markers in patients during migraine and in the interictal phase.

**Methods:** Prospective study (between April 2007 and December 2009) of 47 episodic migraine patients during pain and in the free-headache period (33 without aura and 14 with aura) according to 2004 IHS criteria, and 23 control subjects without any type of headache. Flow-mediated dilatation (FMD), calcitonin gene-related peptide (CGRP), nitric oxide stable metabolites (NOx), vascular endothelial growth factor (VEGF) and endothelial progenitor cells (EPCs) were determined.

**Results:** No changes were observed in FMD between migraineurs and healthy controls (15.3±8.9 vs 17.5 ± 10.1%; p=0.410). An increase in NOx (1225.2±466.1 vs 671.9±358.6 mM; p < 0.0001), CGRP (164.2±139.1 vs 37.1±38.5 mg/ml; p < 0.0001) and VEGF (473.4±398.7 vs 72.6±56.6 pg/ml; p < 0.0001) was observed in migraine patients in relation with controls. EPCs counts were lower in migraineurs (9.4±5.0 vs 17.9±6.0 col/10⁶ cultured cells; p < 0.0001). During attacks, FMD (18.9±12.6%; p=0.381) and VEGF (457.8±271.5 pg/ml; p=0.359) did not statistically differed. NOx (1656.8±259.5 mM; p < 0.0001) and CGRP (298.2±100.3 mg/ml; p < 0.0001) levels were higher and EPCs decreased (7.2±3.2 col/10⁶ cultured cells; p=0.022) during headaches.

**Conclusions:** Endothelial function is altered in patients with migraine and it can be assessed by molecular markers and EPCs in the basal period and during migraine attacks. In our study, ultrasonography did not prove efficacy to show dysfunction of the endothelium.

**PSI-188**

**Advice alone vs. Structured detoxification programmes for complicated medication overuse headache; a prospective, randomized, open-label trial**

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The aim of this study was to compare the effectiveness of advice to withdraw the overused medication with the effectiveness of two structured detoxification strategies in a cohort of patients diagnosed with complicated MOH plus migraine.

One-hundred and thirty seven complicated MOH patients participated in the study. MOH was defined as complicated in patients fulfilling at least one of the following criteria:

a) a diagnosis of co-existent, complicating medical illnesses;

b) a current diagnosis of mood disorder, anxiety disorder, eating disorder or substance addiction disorder;

c) a relapse after previous detoxification treatment;

d) social and environmental problems;

e) daily use of multiple doses of symptomatic medications.

Group A (46 patients) received only intensive advice to withdraw the overused medication.

Group B (46 patients) underwent a standard detoxification programme (advice+steroids+preventive treatment).

Group C (45 patients) underwent a standard inpatient withdrawal programme (as in groupB+fluid replacement and antiemetics).

Withdrawal therapy was considered successful if, after two months, the patient had had reverted to an intake of NSAIDs lower than 15 days/month or to an intake of other symptomatic medication/s lower than 10 days/month.

Twenty two patients failed to attend follow-up visits (11 in group A, 9 in group B, 2 in group C, p=0.03). Overall, we were able to detoxify 70 % of the whole cohort, 60.1% of patients in group A and group B, and 88.8% of those in group C (p < 0.05).
Inpatient withdrawal strategy is significantly more effective than advice alone and outpatient strategy for complicated MOH patient

PSI-189
Non-pharmacologic acute treatment of chronic migraine patients by transcranial cerebral electrical stimulation vs. Placebo
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Background and aims: Stimulation of β-endorphins release from the antinociceptive system by means of electrical alternative current with electrodes placed on the scalp is a known non-invasive method of pain relief. The aim of our study was to estimate the efficiency of transcranial cerebral electrical stimulation (TCES) in the acute treatment of chronic migraine patients vs. placebo.

Methods. We conducted a study on 62 patients diagnosed with chronic migraine (CM) according to the IHS criteria: 47 of them treated by TCES and 15 - by an active placebo device. Dynamic pre- and post-treatment analyses of headache intensity on visual analogue scale (VAS) and serum β-endorphin levels were determined.

Results: Both treatments, by TCES and active placebo, leaded to a significant decrease of pain level on VAS (by 54.2%) and a significant increase of β-endorphin level in 47% of patients. By contrast, in the rest of 53% patients there was a decrease of β-endorphin level after treatment. The following clinical signs were found to be associated with β-endorphins decrease after TCES: younger age at disease onset, longer disease duration, reduced personality anxiety, family history of migraine and more frequent cephalic allodynia. In patients treated by an active placebo device there was a significant decrease in pain intensity without a correspondent increase of serum β-endorphin level.

Conclusions: TCES may be used as a safe non-pharmacologic method of treatment of chronic migraine patients due to its effect on pain reduction and increase of serum β-endorphin level.

PSI-190
Clinical response to onabotulinumtoxina injection therapy for treatment-refractory chronic migraine: “real world” experience
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Background and aims: Large-scale clinical trials have demonstrated onabotulinumtoxinA (onabotA) injection therapy to be safe and effective in treating the chronic migraine population as a whole, but relatively little is known concerning treatment response in the subpopulation of CM patients whose headache disorders previously have failed to respond to multiple prophylactic therapies.

We sought to determine the effect of onabotA therapy in a series of patients with treatment-refractory CM (TRCM).

Methods: We evaluated a series of patients with CM presenting to a university-based headache center and selected from that group a consecutive series of patients with TRCM (defined as per proposed ICHD criteria). Using the PREEMPT dosing/injection paradigm, we treated those patients with open-label onabotA and compared their clinical response to that of a series of CM patients whose headache disorders did not meet criteria for “treatment-refractory”. A positive treatment response was defined as a 50% or greater reduction in headache days/month within the 5th month of the treatment period relative to the pre-treatment baseline month.

Results: We evaluated and treated 168 patients with TRCM and 32 patients whose CM did not meet the proposed criteria for “treatment-refractory”. Sixty-seven (40%) of the 168 TRCM patients achieved a positive treatment response (vs 14/32¼44% in the “non-refractory” group). An additional 41 (24%) in the TCRM group failed to meet the primary endpoint but experienced treatment responses considered sufficiently positive to justify continued injection therapy.

Conclusions: For many patients with TRCM, treatment with onabotA will prove safe and effective.

PSI-191
Suppression of treatment-refractory chronic migraine with low dose methadone: clinical response to a uniform “bridging” protocol
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Background and aims: Chronic migraine often fails to respond to “conventional” therapy. Published results from
studies evaluating treatment of chronic headache with continuous opiate/opioid therapy have been conflicting.

We sought to evaluate the clinical response of patients with treatment-refractory chronic migraine (TRCM) whom we treated with low dose methadone according to a uniform “bridging” protocol.

**Methods:** In a series of patients with TRCM we initiated treatment with methadone and advanced dosage to a maximum of 10mg TID over the subsequent 60 days. A positive initial clinical response was defined as a) no side effects contraindicating continued treatment, b) no over-use of symptomatic medication, and c) a 50% or greater reduction in headache days/month in the third treatment month relative to the baseline pre-treatment month. We continued responders on methadone and added a “conventional” oral agent for prophylaxis. At the 5 month visit, we continued those who continued to exhibit a favorable clinical response on the “conventional” agent and tapered all patients off methadone. The primary outcome variable: successful discontinuation of methadone with sustained clinical improvement during the 1st month off methadone.

**Results:** We evaluated and treated 130 patients according to the protocol described. Fifty-two (40%) met the criteria for a positive response at 3 months. Of these 52 “initial responders, only 4 (8%; 3% of all patients) met the criteria for a positive clinical outcome; in all the remaining 48 patients, headache profiles rapidly worsened following discontinuation of methadone.

**Conclusion:** “Bridge” therapy with methadone is seldom effective in the TRCM population.

**PS1-192**

**Migraine specific cervical tender points during the interictal period of frequent migraine; clinically detectable and treatable phenomenon of trigemino-cervical sensitization**

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**Purpose:** Central sensitization of migraine causes hyperalgesia in trigeminal and cervical territory. This study was to identify the “migraine specific tender points” (MSTP) in the posterior neck during the interictal period. The effect of stretching exercise to reduce tenderness was also investigated.

**Methods:** Seventy-six patients with frequent migraine (4 attacks or more monthly) were studied. Controls were 26 patients with tension-type headache. MSTP and other tender points in the posterior neck were studied by manual palpation. Examiners were blinded for the type of headache and pre- or post-stretching exercise.

**Results:** MSTP was confirmed at lateral sides of both splenius muscles at C3 level. Among 76 patients with migraine during interictal periods, MSTP was found in 72 patients (95%). Sixty-five per cent complained severe, sharp pain, and 35% experienced radiation of pain to the side of the headache. Among 26 patients with tension-type headache, 6 patients (23%) showed MSTP (significantly less than migraine p < 0.001), but 23 patients (88%) presented with other multiple tender points with small nodular muscle contraction in the posterior neck. Stretch exercise by rotating the shoulders horizontally without moving the neck axis relieved MSTP to less than 50% in 74 patients (97%). During migraine headache (N=6), patients felt intense, sharp MSTP which referred to the region of headache.

**Conclusion:** Sustained sensitization in the trigemino-cervical system during the interictal period of frequent migraine caused severe tender points at the periphery of cervical nerves. The reduction of MSTP by stretching exercise indicated the inhibitory trigemino-cervical convergence mechanism.

**PS1-193**

**Endovenous in-hospital desensitization and detoxification of chronic migraine and medication-overuse headache**

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**Background and aims:** In recent years, central sensitization has reached a great importance in migraine chronification. In animal and clinical studies most oral treatments have failed to treat these models or patients. Just a few group of drugs have shown efficacy if given endovenously when central sensitization is present: valproate, NSAID’s, methoclopramide. In present study we want to analyse our experience with such treatments in a clinical setting.

**Methods:** In last 4 years we have used the same protocol treatment for in-patients with Chronic Migraine (CM) with or without Medication Overuse Headache (MOH): endovenous Valproate continuous infusion (1600-2000 mg/day, 4-5 days) + ketorolac + tiapride pulses (3xday, decreasing in 4-5 days). We review all patients in terms of efficacy, outcome and adverse events. Previous and follow-up preventive treatments are analysed.

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Results: 36 patients were treated with this protocol, 31 with CM +/− MOH (20 MOH). 27 patients (87.1%) showed great improvement, most of them complete (25) and 4 (12.9%) did not improve. It was generally well-tolerated, just 3 patients referred notorious adverse events, one of them with a reversible hyperammoniemic encephalopathy. Some patients (5) needed new in-patient treatment after +/- 1.5 years. The general outcome was positive, most of them with 1-2 preventive drugs in follow-up visits (topiramate, beta-blockers,...).

Conclusions: Endovenous valproate + ketorolac + tia-pride seems a good ‘desensitizing’ treatment in these difficult-management refractory patients. Adverse events are not usual and are mild. When out-patient treatment fails, we need special approaches to manage this kind of patients.

PS1-194
Capsaicin stimulation causes caspase-2-dependent apoptosis: relevance to the chronification mechanism of migraine
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Objective: TRPV1 (transient receptor potential vanilloid subfamily 1) is a cation channel critically associated with nociception. As TRPV1 function is enhanced by inflammatory mediators, neurogenic inflammation associated with migraine attacks is expected to sensitize TRPV1. We demonstrated that TRPV1 agonist stimulation under the TRPV1 overexpressing state causes caspase-dependent apoptosis and that there is little contribution of capsase-3 to this apoptotic process. Degeneration of sensory neurons is implicated in the development of neuropathic pain, which may contribute to chronification of pain disorders. In this study, we explored the involvement of caspase-2 in the TRPV1-mediated apoptosis.

Methods: We used PC12 cell lines stably expressing TRPV1 at differing levels. Capsaicin (50 mM) was used to stimulate TRPV1. C-terminally V5-labeled caspase-2 was overexpressed in these cells, and caspase-2 cleavage that concurs with its activation was examined. We performed the TUNEL assay to detect apoptosis, and examined whether pharmacological caspase inhibition could block the occurrence of apoptosis.

Results: In TRPV1 high expressing cells, caspase-2 cleavage became obvious at 3 hours of capsaicin treatment. Such caspase-2 processing was not observed in TRPV1 low expressing cells. Besides, the occurrence of apoptosis was time-dependent, such that the number of TUNEL-positive cells increased after 3 hours of capsaicin treatment. Z-VD(OMe)VAD(OMe)-FMK, a caspase-2 inhibitor, was effective in preventing the occurrence of apoptosis with a higher potency than the pan-caspase inhibitor, Z-VAD-FMK.

Conclusion: We clarified that caspase-2 is responsible for TRPV1-mediated apoptosis. Our findings suggest that caspase-2 may be a novel therapeutic target for chronic pain disorders including migraine.

PS1-195
Repetitive transcranial magnetic stimulation modulates the nociceptive-specific blink reflex in healthy subjects but not in migraineurs
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Background: The link between cortical phenomena and trigeminovascular activation remains unclear in migraine. Visual stimulation and cortical spreading depression (CSD) in the visual cortex were shown to increase excitability of 2nd order trigeminal neurons in animals.

Objective: To search for a functional connection between visual cortex and trigeminal nociceptive system in healthy volunteers (HV) and migraine without aura patients (MO).

Methods: 22 HV and 13 MO underwent nociceptive blink reflex (nBR) recordings before and after 1Hz and 10Hz repetitive transcranial magnetic stimulation (rTMS) of the visual cortex. We measured pain thresholds (PT), R2 area under the curve (AUC), and calculated R2 habituation and slope. We also performed the same study in HV after 8Hz visual flash stimulation.

Results: In HV, PT decreased after 1Hz and 10Hz rTMS (p = 0.0019, p = 0.046), R2 AUC increased bilaterally after 1Hz (p = 0.024, p = 0.036) whereas it decreased after 10Hz rTMS. In MO, R2 AUC decreased after 10 Hz rTMS. Habituation was increased contralaterally in HV and MO after 1Hz rTMS (p = 0.002, p = 0.004). Visual stimulation in HV produced the opposite of 1Hz rTMS: increase in PT, decrease in R2 AUC.
**Conclusions:** For the first time we demonstrate a functional connection between the visual cortex and the trigeminal nociceptive system in humans. The modifications found after 1 Hz rTMS -supposed to inhibit the underlying cortex- are in line with those observed during migraine attack and CSD in animals. Why changes are not significant in MO (though in the same direction) could be related to the interictal dysexcitability found in migraine.

**PSI-196**

No effect of a 1 hour sub-occipital transcutaneous stimulation on the nociceptive blink reflex in healthy subjects

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**Background:** Subcutaneous occipital nerve stimulation was found effective in refractory cluster headache and chronic migraine, but not in all patients. Up to now, no clinical characteristics predicting response have been identified. The effect of transcutaneous occipital nerve stimulation (tONS) on the nociceptive blink reflex (nBR) could have such predictive value.

**Objective:** To search in healthy volunteers for an effect on the nociceptive blink reflex of prolonged suboccipital transcutaneous stimulation using an adaptation of the Cefaly® device (STX-Med, Belgium).

**Methods:** Fifteen bilateral nBR responses were recorded by stimulating the right supraorbital nerve at 1.5 times the pain threshold in 10 healthy subjects before and immediately after 1 hour of tONS (frequency 100 Hz, mean intensity 17.4 mA, current dose 1.56 uC). We determined sensory and pain thresholds, and measured the R2 area under the curve (AUC) on 3 consecutive blocks of 5 responses. Habituation was defined as the slope of the linear regression line for the 3 successive blocks.

**Results:** Sensory and pain thresholds, nBR R2 AUC and habituation were not significantly modified after tONS during 1 hour.

**Conclusion:** These findings suggest that prolonged transcutaneous suboccipital stimulation does not modify excitability of the brainstem trigeminal neurons involved in the nociceptive blink reflex. It remains to determined whether results are similar in headache patients and whether tONS is able to modify the cortical processing of trigeminal nociceptive input.

**PSI-197**

Genome-wide association study reveals three susceptibility loci for common migraine in the general population

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**Objective:** Migraine is a common, heterogeneous, and heritable neurological disorder. The pathophysiology is incompletely understood and genetic influences at the population level are unknown.

**Methods:** We performed a genome-wide association analysis in a North American population-based cohort (WGHS: 5122 migraineurs/18,108 non-migraineurs). Two other population-based cohorts from the Netherlands and Germany (GEM: 774/942; SHIP: 306/2260) and a clinic-based international case-control sample (IHGC: 2748/10,747) served as replication. All participants were of European ancestry.

**Results:** Among the SNPs prioritized in the WGHS, SNPs at three novel loci were significant in meta-analysis among the three replication cohorts. Genome-wide significance was achieved in meta-analysis combining all cohorts. Further analyses in the WGHS suggested that two of the SNPs showed associations specific for migraine as compared to non-migraine headache. All three associations were similar for migraine with aura and without aura and none of the SNPs was specific for any migraine feature (e.g. pain location, pain quality, nausea/vomiting).

**Conclusion:** We have identified SNPs at three novel loci with genome-wide significant association for migraine at the population level. All are distinct from the association at 8q22.1 reported by a recent genome-wide study in a
clinic-based cohort, potentially emphasizing differences between population-based compared with clinic-based migraine. One of the novel loci integrates with the potential role of glutamate in migraine pathophysiology while a second novel locus may be linked to the pain aspect of migraine. A lack of differential associations for migraine with and without aura may suggest shared pathophysiology for the two major subtypes of migraine.

**PSI-198**

**Nitric oxide modulation of low frequency oscillations in cortical vessels in familial hemiplegic migraine - a near infrared spectroscopy study**


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**Background and Aims:** The functional consequences of gene mutations in patients with familial hemiplegic migraine (FHM) are not known. We investigated changes in low frequency oscillations (LFO) of cortical vessels in response to nitric oxide donor glyceryl trinitrate (GTN) by near infrared spectroscopy (NIRS) in FHM patients.

**Methods:** 23 FHM patients without known mutations and 9 healthy controls received a continuous intravenous infusion of GTN 0.5 μg/kg/min over 20 min. Using NIRS we recorded oxygenated hemoglobin LFO at baseline and 15 and 40 min after start of GTN infusion.

**Results:** GTN changed LFO amplitude in FHM patients (P = 0.002) but not controls (P = 0.121). In FHM patients with co-existing migraine with and without aura we found significant changes in LFO amplitudes after GTN infusion (P < 0.001). Post-hoc analysis revealed an increase in LFO amplitude 15 (P = 0.003) and 40 (P = 0.013) min after start of infusion compared to baseline. There were no changes in LFO in patients with a pure FHM phenotype (P = 0.695).

**Conclusions:** We found an increase in cortical vessel LFO amplitudes in response to GTN in FHM patients with a pure phenotype. However, only FHM patients with a mixed phenotype showed increased arterial responses. These data add to the growing evidence for distinct pathophysiological mechanisms in the migraine spectrum.

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neurogenic dural plasma protein extravasation (PPE) in
guinea pigs does not seem to reflect the chronic migraine
 genesis, because of its rapid onset of the attack inducing
after application of drug meta-chlorophenylpiperazine
(mCPP). Interestingly, unlike guinea pigs, the same dose
of mCPP is not able to induce a dural PPE in mice. On
the other hand mice have been shown an enhanced activa-
tion of 5-HT2B receptors after a chronic hypoxic treat-
ment that is a limiting step required for vascular cellular
alterations in a pulmonary hypertension mouse model.
Therefore we have tested the mCPP-induced dural PPE
in the mouse model, and found that chronic hypoxia
leads to an induction of dural PPE by mCPP, which was
similar in guinea pigs. More important, the application
of the 5-HT2B receptor selective antagonist, BF-1 during the
hypoxia, could completely reverse the hypoxia induced
susceptibility of the dural PPE indicating that activation
5-HT2B receptors during the hypoxia is essential for de-
velopment of this susceptibility. Chronic hypoxic treatment
might cause vascular alterations in the mouse dural blood
vessels comparable to those shown in pulmonary blood
vessels under the same condition. Our data is also in
agreement with the fact that migraine prevalence is
increased in high-altitude populations. Therefore the for-
mation of this susceptibility of dural PPE in response to
mCPP in hypoxic mice.

Subsequently, we investigated the effects of pharmacologi-
cal proteasome and lysosomal protease inhibition on the
expression levels of TRPV1.

Results: BoNT-A decreased the plasma membrane
TRPV1 trafficking in TGN. Concomitantly, the total
TRPV1 expression was reduced. There was no discernible
effect of BoNT-A application on TRPV1 transcription. The
steady-state expression level of Y200F TRPV1 was lower
in PC12 cells than that of wild-type TRPV1. Proteasome
inhibition increased both wild-type and Y200F mutant
TRPV1 expression levels with a much greater effect on
the latter.

Conclusion: BoNT-A inhibits TRPV1 trafficking to the
plasma membrane and reduces the total TRPV1 expres-
sion by a post-transcriptional mechanism in the TGN.
TRPV1 appears prone to intracellular proteasomal degra-
dation, unless it is properly mobilized to the plasma mem-
brane. Modulating TRPV1 plasma membrane trafficking
may account for the efficacy of BoNT-A against chronic
migraine.

PSI-202
Cortical spreading depression attenuates
hippocampal long-term potentiation via post-
synaptic mechanism

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The association between transient global amnesia and
migraine has long been documented. Although the
mechanism underlying this phenomenon is still unclear,
the alteration of hippocampal neurotransmission by corti-
cal spreading depression (CSD) is a possible explanation.
The present study was conducted to determine the
mechanism by which CSD affects the generation of long-
term potentiation (LTP) in hippocampus. The CSD was
induced in Wistar rat brains by direct application of KCl
on frontal cortex. After completion of 45-minute CSD
recording, rat brains were removed for preparation of
hippocampal slice. Field-potential recordings were made
in the pyramidal cell layer of the CA1 region. The stimulus
strength was adjusted so that excitatory postsynaptic
potentials (EPSPs) of 0.10 - 0.15 mV/ ms slopes and popula-
tion spikes of 0.7 -1.2 mV in amplitude were evoked. The
results showed significant decrease in LTP amplitude in the
CSD group. To investigate whether CSD affected presyn-
naptic release probability at Schaffer collateral (SC)-CA1
synapses, we measured the pair-pulse facilitation (PPF)
index of fEPSPs. The result showed that no difference in
PPF profile between CSD and control slices. We, then, measured input/output (I/O) curve of AMPA receptor-mediated fEPSPs to determine the involvement of this postsynaptic receptor in the process. The result showed that AMPA receptor-mediated fEPSP I/O curve was significantly reduced in hippocampal slices obtained from CSD rats (P = 0.033). This result indicated that CSD depressed the glutamatergic transmission at SC-CA1 synapses. This alteration may explain the amnesic phenomenon occurs during the attack of migraine-related transient global amnesia.

PS1-203
Cortical spreading depression is modulated by 5-ht1B/1D receptor agonist naratriptan
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Background and aims: Naratriptan, a serotonin 5-HT1B/1D receptor agonist, is an effective and widely used drug for the acute treatment of migraine. The effects of naratriptan on direct current (DC) shift and cortical blood flow (CBF) changes seen with cortical spreading depression (CSD) have not been determined. This study was conducted to investigate whether naratriptan alters DC shift or CBF changes induced by CSD.

Methods: Male Sprague-Dawley rats (300-350g) were separated into two groups, control and naratriptan (n = 6, each). In both groups CSD was induced by topical application of 3 mg KCl on the frontal cortex. After inducing one CSD and the recording of the respective DC shift and hyperemia, naratriptan (5 mg kg\(^{-1}\) body weight, i.v.) or saline (control group) was administered and DC shift and CBF were recorded using a glass microelectrode and laser Doppler flowmeter, respectively, for one hour.

Results: Naratriptan significantly reduced the frequency and amplitude of DC shift (p < 0.05). CSD frequency was reduced from 15±2 peaks in one hour in the control group to 10±2 peaks in one hour in the naratriptan group. The amplitude of DC shift was significantly reduced from 14.1±3.1 mV in the control group to 10.7±5.0 mV in the naratriptan group (p < 0.05). CBF changes showed no significant difference.

Conclusion: The results show for the first time that the 5-HT1B/1D receptor agonist, naratriptan decreases the CSD frequency and amplitude in an in vivo animal model relevant to some parts of migraine.

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PS1-204
Microinjection of lidocaine in nuclear raphe magnus increases stimulus-evoked trigeminal cell firing in the trigeminocervical complex
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Background and aims: A change in the downstream pain control systems may be an important component of the pathophysiology of migraine. Nucleus raphe magnus (NRM) has been implicated in pain control more generally leading to an interest in its possible role in migraine. This study was conducted to determine the effect of lidocaine microinjection into NRM on trigeminovascular activity in response to middle meningeal artery (MMA) stimulation.

Methods: Adult male Sprague-Dawley rats were anesthetized with pentobarbitone sodium (60 mgkg\(^{-1}\)). The anesthesia was maintained using intravenous propofol (20 mgkg\(^{-1}\)h\(^{-1}\)). The parietal bone was removed over the MMA for stimulation with a bipolar electrode. For recording trigeminocervical neuronal activity, the tungsten electrode was inserted into the trigeminocervical complex. Lidocaine (100 nl, 2%) was microinjected with pontamine sky blue into NRM, with saline as the control (100 nl). The effects of lidocaine and saline were recorded and compared over 60 minutes after the injection.

Results: Microinjection of 100 nl of 2% lidocaine significantly increased cell firing in response to trigeminovascular activation compared with saline group (p < 0.05). This activation was significant ten minutes after lidocaine injection with a maximum effect after 75 minutes.

Conclusion: This study suggests that the inhibition of NRM may increase the neuronal activation with nociceptive trigeminovascular stimulation. Understand how the NRM modulates trigeminovascular neurotransmission will improve understanding of the pathophysiology of migraine.

PS1-205
Rapid eye movement sleep behavior disorder-like symptoms in migraine patients: questionnaire-based case control study
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**Background:** Rapid eye movement sleep behavior disorder (RBD) is characterized by dream-enacting behaviors during rapid eye movement sleep. Although sleep disorders have been associated with patients with migraine, the association between RBD and migraine has not been evaluated.

**Methods:** A cross-sectional, case-control study was conducted, including patients with migraine (n=262, mean age 38.2 years) and headache-free control subjects (n=163, mean age 37.3 years). RBD screening questionnaire Japanese version (RBDSQJ) was used and subjects who scored 5 or greater were defined as having RBD-like symptoms (RBD-s). All participants completed the Migraine Disability Assessment (MIDAS) questionnaire, Beck Depression Inventory scores (BDI)-II, Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS). A total of 210 blood samples were collected to correlate various parameters with RLS.

**Results:** Migraine patients showed a significantly increased frequency of RBD-s compared to that in controls (21.8 % vs. 12.9 %). Subset analysis included subjects with under age 50 years showed an increased frequency of RBD-s in migraine patients compared with that in controls (25.0 % vs. 14.3 %), while among subjects aged 50 years or older, the frequency did not reach statistically significance (8.0 % vs. 4.3 %). Migraine patients with RBD-s were younger and had higher score of MIDAS, BDI-II, PSQI, and ESS than those without. With regard to the medication, antidepressant use was similar in both groups, though minor tranquilizers use was more frequent in migraine patients with RBD-s than those without.

**Conclusion:** Our study results suggest a positive association between various factors in migraine such as headache-related disability, depressive symptoms, sleep disorders, and RBD-s.

**PS1-206**

**Comorbidity and causal factors of restless legs syndrome in migraine patients**

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**Backgrounds:** Recent studies have provided evidence for a positive association between migraine and restless legs syndrome (RLS), although the exact mechanisms and factors remain unclear.

**Methods:** A cross-sectional, case-control study was conducted, including patients with migraine (n=262) and headache-free control subjects (n=163). Migraine was diagnosed according to International Classification of Headache Disorders II criteria. RLS diagnosis was made based on four essential criteria as described by the International Restless Legs Syndrome Study Group. All patients completed the Migraine Disability Assessment (MIDAS) questionnaire, Beck Depression Inventory scores (BDI)-II, Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS). A total of 210 blood samples were collected to correlate various parameters with RLS.

**Results:** RLS frequency was significantly greater in patients with migraine than in controls (13.7% vs. 1.8%, P < 0.0001). Migraine patients with RLS had high scores for MIDAS, BDI-II, PSQI, and ESS compared with those without RLS. In addition, migraine patients with RLS had a high rate of smoking and RLS family history, as well as increased levels of serum phosphorus and urea nitrogen compared with those without RLS. In migraine patients, logistic regression analysis revealed that positive RLS family history, BDI-II, ESS, and serum phosphorus levels were significant RLS predictors.

**Conclusion:** Our study confirmed a positive association between RLS and migraine. RLS co-morbidity in migraine patients was associated with insomnia, daytime sleepiness, depressive symptoms, headache-related disability, and increased serum phosphorus levels. These findings may provide a better understanding of RLS pathogenesis in migraine.

**PS1-207**

**A case of hemimasticatory spasm misdiagnosed as trigeminal neuralgia**

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**Background and aims:** Hemimasticatory spasm (HMS) is a rare disorder characterized by involuntary contraction of muscles innervated by the motor root of the trigeminal nerve. We report a case of HMS that was initially misdiagnosed as trigeminal neuralgia (TN).

**Methods:** Case report.

**Results:** A 64 year-old woman presented with severe paroxysmal pain in the right jaw (temporomandibular region to lower right mouth). Each paroxysm lasted a few seconds sometimes followed by a dull ache for 30-60 seconds. In addition to spontaneous episodes, triggers included chewing, cold temperature, bending over, blowing her nose, and talking. Initially, episodes occurred 2-3 times/day, but increased in frequency. Due to pain, the patient
avoided chewing and other jaw movements. TN was diagnosed. Carbamazepine, up to 200 mg TID, and baclofen, up to 80 mg TID, resulted in modest improvement. Higher doses were limited by intolerance.

The patient was subsequently seen at our institution. The pain was described as a “charley horse” (cramping), occasionally associated with involuntary jaw closure. Exam demonstrated involuntary spasms of the right masticatory muscles and right masseter atrophy. EMG during clinical spasm showed tonic activity in bilateral masseter muscles. blink reflexes showed relative prolongation of right R1 with absent jaw jerk, consistent with right trigeminal neuropathy. Brain MRI was unremarkable.

The HMS has been successfully treated with serial onabotulinumtoxinA injections for 12 years.

Conclusion: HMS is a rare cause of paroxysmal facial pain that should be considered when patients present with symptoms suggestive of TN. It can be successfully managed with onabotulinumtoxinA.

PSI-208

A new treatment of chronic post-traumatic headache by epidural saline and oxygen injection: an application of old diagnostic method

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Introduction: Chronic post-traumatic headache (CPTH) is still a common complication of minor injuries and effective treatment has not yet been available up to now. Epidural blood patching has been reported effective but its effectiveness is limited. Before the era of MRI, air epidurography was performed and it was used as a treatment for lumbago (Zentralbl Gynakol 300; 75, 1953). We applied this method to treat CPTH with some modification.

Method: Nineteen cases with CPTH for over 3 months were treated. The modification of air epidurography was that the air was replaced by oxygen and saline was added. The effectiveness of epidural saline and oxygen injection (ESOI) was evaluated after 3 months; Excellent (return to normal life almost), Good (diminished headache but still disturbed normal life), Fair (diminished headache with recurrence), No (no effectiveness), and Poor (worsen headache). Results were demonstrated in mean +/- SD.

Results: Mean age was 38.1 +/- 13.7 yo. Mean duration of illness was 53.8 +/- 72.3 months ((4 to 228 months). Types of injuries were traffic accident (14 cases), violence (4 cases), and fall (1 case). The result of the treatment after 3 months was as follows; Excellent (12), Good (5), and Fair (2). In three cases, eye symptoms were improved and the improvement of accommodation function were verified objectively by means of TirIRIS (Hamamatsu Photonics, Japan). There was no worsened case.

Conclusion: ESOI is a new and safe treatment modality for long lasting CPTH. The effectiveness can be verified objectively by measuring eye function.

PSI-209

The relationships between topographical eeg and clinical backgrounds among migraine patients

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This study aimed to investigate the relationships between clinical parameters of migraineurs and topographical EEG changes during the photic driving responses.

We studied 28 patients (male/female=9/19, age 20-50, migraine with aura/migraine without aura =11/17) who had a checkup at outpatient and diagnosed as migraine with the diagnostic criteria of International Classification of Headache Disorder II.

We recorded spontaneous eyes-closed resting EEGs from 20 electrodes on the scalp. Stroboscope flashes consisting of 3-5-8-10-13-15-18-20 Hz were used. After recording, 3 artifact-free EEG epochs consisting of 2.56 ms during photic stimulation were selected. The selected EEGs were analyzed by FFT and we observed the frequency peaks and its topographies. The gravity center, center point of positive and negative areas of the topography, was used to assess 2 dimensional changes for each driving response. The correlation with a clinical background such as duration of illness, age of onset, and subtypes of migraine was examined for the global field power (GFP) value and the gravity center. The gravity center shifted anterior from fundamental driving to harmonic driving for each photic frequency. This anterior shift was more evident for longer duration of illness, although no significant differences between subgroups. The GFP value had a positive correlation between the duration of the illness. Anteriorisation is caused by longer disease duration regardless of the different subgroup. This might reflect generalized central sensitization caused by disclosure of pain. Our examination might prove abnormal perceptual process for photic hypersensitivity of migraine.
PSI-210

Body mass index (BMI) and migraine days: survey in a Japanese headache center

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Chronification of migraine headache is one of the most urgent issues in headache management. We analyzed possible association of migraine chronification and obesity in a Japanese Headache Center.

Subjects and methods: We have examined 1255 headache sufferers from February 2010 to January 2011. We interviewed all patients with structured questionnaires. Type of headache was determined in accordance with ICHD-II. 685 subjects had migraine headache. Height and body weight were recorded. According to BMI, subjects were categorized to five ranks, i.e., underweight (BMI < 18.5), normal (18.5-24.9), overweight (25-29.9), obese (30-34.9), and morbid obese (>35). Average headache days and migraine days of recent three months were recorded. Frequency of acute medication use was also recorded. The data were analyzed with chi-square test and one-way ANOVA.

Results: 40 out of 129 underweight migraineurs (31.0%), 148 of 451 normal-weight ones (32.8%), 42 of 82 overweight ones (51.2%), 9 of 19 obese ones (47.4%), and 3 of 4 morbid obese ones (75.0%) had more than 15 headache days and 8 migraine days (p = 0.003, Pearson's chi-square test). Mean headache days were 14.7 ± 1.0 (SE), 13.2 ± 0.5, 14.8 ± 1.2, 15.2 ± 2.3 and 20.0 ± 6.1 days/month in underweight, normal, overweight, obese and morbid obese migraineurs, respectively (p = 0.37, ANOVA). Mean migraine days were 5.9 ± 0.5, 6.1 ± 0.2, 8.2 ± 0.7, 8.8 ± 1.4 and 12.5 ± 3.2, respectively (p < 0.001, ANOVA).

Conclusion: Overweight or obese migraineurs tended to have more migraine days than normal or underweight migraineurs in a Japanese series.

PSI-211

Serum interleukin-6 and adiponectin levels in migraineurs

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Background: There are some evidences suggesting that an immunologic dysfunction has been hypothesized to be involved in migraine pathogenesis. It is not yet clearly understood what immunological mechanism leads to migraine headaches.

Objectives: The aim of this study was to investigate the serum Inteleukin-6 (IL-6) and adiponectin (Ad) levels in patients with migraine.

Methods: IL-6 and Ad levels in serum were measured in 15 patients with migraine with aura (MA; 5 males and 10 females, average age: 31.5 years) and 31 patients with migraine without aura (MO; 8 males and 23 females, average age: 39.4 years). Thirty normal healthy volunteers composed the control group (CTL; 11 males and 19 females, average age 44.6 years). IL-6 and Ad levels in serum were determined respectively using chemiluminescence enzyme immunoassay and latex immunology turbidimetric method.

Results: Mean IL-6 levels in serum were 19.1 pg/mL in the patients with MA, 11.7 pg/mL in the patients with MO and 1.7 pg/mL in CTL. IL-6 level in the patients with MA was significantly higher than in the MO and CTL (p = 0.0228). Mean Ad levels in serum were 10.3 ug/mL in the patients with MA, 9.5 ug/mL in the patients with MO and 11.4 ug/mL in CTL. Ad level in MA, MO and CTL was not significantly different.

Conclusion: Some cytokines have recently been shown to have pain-mediating functions, in addition to their known immunological functions. Our results suggest that antibody-mediated immunity associated with IL-6 is involved in migraine pathogenesis.

PSI-212

Role of cannabinoid receptors in hyperalgesia induced by nitroglycerin: study in animal model of migraine

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Experimental animal models exploring the effects of nociceptive activation of the trigeminovascular system and aimed to understand the pathophysiology of migraine have suggested the existence of several interactions between the endocannabinoid system and pain mediation in migraine. Extensive evidence have demonstrated a role for the CB(1) receptor in the antinociception.
However, recent research suggests that also CB(2) receptors, especially located outside the central nervous system (CNS), play a role in the perception of pain. In this study we evaluated the role of cannabinoid receptors in a well-known animal model of migraine based on the hyperalgesia induced by nitroglycerin administration at the tail flick. The test was performed in male Sprague-Dawley rats that were pre-treated with nitroglycerin (10mg/kg, i.p.) or saline (4 hours before) and treated with CB1 antagonist (AM251, 4mg/kg i.p.) or CB2 agonist (AM1241, 4mg/kg, i.p) 60 minutes before the experimental tests. The findings have shown that both molecules have a significant analgesic effect in baseline conditions. While, CB1 antagonist abolished nitroglycerin-induced hyperalgesia at the tail flick test, administration of CB2 agonist did not shown any analgesic effect. These findings demonstrate that CB1 receptor antagonist at high doses can have analgesic effects in both baseline condition and nitroglycerin-induced hyperalgesia. While, CB2 receptor agonist at the same dose have analgesic effect only in baseline conditions. The data suggest that pharmacological manipulation of the CB1 receptor may have therapeutic potential in the treatment of migraine.

**PS1-213**

**Headache features in moh patients following detoxification - use of an electronic diary**

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Using an electronic diary associated with an assisted diagnosis feature, we describe the clinical phenotype of headache attacks in subjects with MOH who successfully underwent detoxification.

Five hundred and 25 subjects suffering from chronic headache who were overusing acute drugs underwent standardized in-patient or out-patient detoxification procedure.

Four hundred and 95 patients were no longer overusing at 2 and 6 months following detoxification.

Primary headache was episodic migraine without aura in 414 subjects, episodic or chronic tension-type headache in 83 subjects, mixed in the remaining subjects.

Analytical evaluation of the individual attacks with the electronic diary showed that patients originally diagnosed as suffering from chronic tension-type headache also presented migraine attacks following detoxification. Conversely, patients originally suffering from migraine without aura also suffered from tension-type attacks following detoxification. Furthermore, patients suffering from migraine without aura showed significantly less headache days in the 6 months following detoxification when compared to patients suffering from tension type headache as primary headache.

The use of specific diaries is recommended for diagnostic as well as for management purposes in patients recovering from MOH.

**Acknowledgements:** COMOESTAS Project - EC contract number 215366 (COMOESTAS) FP7 - Thematic priority ICT

**PS1-214**

**Is the dose-response of telcegepant well characterized?**

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The doses used in most randomised, controlled trials (RCTs) with telcagepant are 140/150 mg 280/300 mg. The results for the two doses are shown in the table:

<table>
<thead>
<tr>
<th></th>
<th>Ho et al 2008</th>
<th>Connor et al 2009</th>
<th>Ho et al 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain freedom</td>
<td>26.0% (n = 353)</td>
<td>23.8% (n = 371)</td>
<td>25.1% (n = 534)</td>
</tr>
<tr>
<td>280/300 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain freedom</td>
<td>17.2% (n=331)</td>
<td>23.2% (n=381)</td>
<td>21.9% (n=556)</td>
</tr>
<tr>
<td>140/150 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain relief</td>
<td>55.0% (n = 353)</td>
<td>55.6% (n = 371)</td>
<td>56.7% (n = 534)</td>
</tr>
<tr>
<td>280/300 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain relief</td>
<td>49.8% (n = 331)</td>
<td>53.9% (n = 381)</td>
<td>58.6% (n = 556)</td>
</tr>
<tr>
<td>140/150 mg</td>
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</tbody>
</table>

For pain freedom at 2 h, a primary endpoint, telcegepant 280/300 mg (mean = 25.2%) was superior to telcagepant 140/150 mg (mean = 21.0%) (p< 0.05, effect size 4.2% (95%CI: 0.9% to 7.4%)). Telcegepant 280/300 mg (mean = 55.9%) was not superior to telcagepant 140/150 mg (mean = 54.9%) (effect size: 1% (95%CI: -2.9% to 4.8%)) for mean pain relief, one other primary endpoints. In one RCT the efficacy of telcegepant 50 mg was intermediate between placebo and the 140/150-mg and 280/300-mg doses [Connor 2009]
In conclusion: The lower part of the dose-response curve for the anti-migraine effect of telcagepant seems fairly well characterized. Based on the two primary endpoints, pain freedom and pain relief at 2 h, the doses of 140/150-mg and 280/300-mg seem somewhat equivalent with some advantage for the 280/300-mg dose for pain free. The choice of dose cannot be based on tolerability which is excellent.

**PSI-215**

**Migraine and biomarkers of endothelial activation in young women: association with adverse childhood experience**

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**Background:** There is emerging data that childhood adversity is linked to migraine as well as to inflammatory, vascular, and metabolic biomarkers.

**Objectives:** Our objective is to test the relationships of migraine and biomarkers with adverse childhood experiences (ACE).

**Methods:** Vascular and metabolic biomarkers from blood and urine were evaluated in women between 18-50 years, including 125 with migraine (interictal) and 50 without migraine. Confidential data on ACE using a valid and reliable questionnaire (response rate 79%, 100 migraineurs, 41 controls) were collected.

**Results:** The odds of having any abuse were higher for migraineurs (OR=1.53, 95% CI 1.07-2.17). In migraineurs average ACE scores were higher with chronic (3 vs 2, p=.02), continuous (3.9 v 2.2, p=.007) and transformed (3.1 v 2.0, p=.016) migraine, and correlated positively with headache frequency (r=.37, p=.001) and negatively with age of headache onset (-.22, p=.04). In the entire cohort, for those with ACE ≥1, the biomarker levels that were elevated were, CRP (p<.0001), vWF activity (p=.002), tPA Ag (p=.005), F1+2 (p=.02), TGFbeta1 (p=.01), cholesterol (p=.03), triglycerides (p=.008). Decreased biomarker levels were observed for adiponectin (p=.013), and NOx (p=.006). The ACE score correlated positively with BMI (r=.43, p=.0001), CRP (r=.98, p=.0001), vWF activity (r=.21, p=.009), tPA Ag (r=.28, p=.004), TGFbeta1 (r=.28, p=.003), TNF alpha (r=.20, p=.03), IL 6 (r=.22, p=.03), cholesterol (r=.20, p=.04), triglycerides (r=.25, p=.01) and negatively with adiponectin (r=-.29, p=.003).

**Conclusions:** Our findings implicate early life stress as one possible link between migraine and stroke in premenopausal women.

**PSI-216**

**The effect of acute trigeminal activation on CSD threshold**


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**Background and aims:** Although cortical spreading depression (CSD) is a potential migraine trigger, little is known about the factors that can modify the properties of CSD. Here, we examined the relationship between trigeminal activation and CSD occurrence.

**Methods:** Nine Sprague-Dawley rats were used. Under anesthesia, a D.C. electrode was set on the exposed parietal bone. We installed a small open cranial window near the electrode. The dura matter within the cranial window was removed, after which an embankment-like structure was made with dental cement around the cranial window. In the control group of rats, 0.1ml saline was injected into the bilateral whisker pads. Subsequently, 1M potassium was applied to the cranial window to induce CSD. We measured D.C potentials, and analyzed the frequency of negative deflections representing CSD.In the capsaicin-treated group, 10 mM/0.1ml capsaicin was injected into the bilateral whisker pads before inducing CSD. In the vehicle-treated group, only the capsaicin solvent (6% ethanol and 6% Tween80) was administered before CSD induction.

**Results:** During the CSD induction period, the rats in control group exhibited 9.5 ± 3.2 times negative deflections, the capsaicin-treatment group 22.0 ± 1.0 times, and the vehicle-treated group 23.0 ± 4.9 times. The durations of CSD were 65 ± 15 minutes in the control group, 133 ± 17 minutes in the capsaicin-treated group, and 127 ± 23 minutes in the vehicle group.

**Conclusions:** Acute trigeminal activation lowered the CSD threshold. This finding suggests that trigeminal activation predispose migraineurs to increased migraine frequency.
PSI-217

Real life experience of amitriptyline chloridrate plus chlordiazepoxide use for the prophylaxis of migraine

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Background: Migraine, anxiety and depression may share common biological causes since antidepressant drugs are used in migraine prophylaxis. The use of a fixed dose of amitriptyline combined with chlordiazepoxide may be effective for the prophylactic treatment of migraine.

Methods: A real life observational study was conducted among patients of a Headache Center. Patients over 18 years of age were included in the study if they met IHS criteria for migraine and presented two or more attacks per month lasting more than 48 hours and minor depression comorbidity. Tablets with a fixed dose of amitriptyline chloridrate (14,15 mg or 28,3 mg) plus chlordiazepoxide (5 mg or 10 mg) were administered once daily. Follow-up examination was scheduled every three month.

Results: 47 patients (38 W and 9 M) were included. Mean age was 45.9 ± 13.0 years. 26 patients (55%) attended the follow-up examinations while 21 (45%) missed the follow-up examinations and thus were considered drop-out. 7 patients went on 28,3/10 mg and 19 on 14,15/5 mg treatment. Mean duration of treatment was 6.3 ± 3.0 months. 16 patients (61.5%) had a reduction of the number of migraine attacks equal or over 50%, 6 patients (23.1%) had a reduction less than 50%, while 4 patients (15.4%) did not improve.

Conclusions: The results of the present study indicate that the use of amitriptyline combined with chlordiazepoxide is effective for the prophylaxis of migraine. This combination may have a synergistic effect thus permitting to use low dosages and minimizing side effects.

PSI-218

The angiotensin ii receptor 1 gene 1166a>c polymorphism in primary headaches

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Background and aims: Various drugs influencing the renin-angiotensin have been used in the prophylactic treatment of migraine during the last decade, but the reason for their efficacy remains obscure. Studies on common polymorphisms in the angiotensin-converting enzyme (ACE), angiotensinogen (AGT) and angiotensin II receptor I (AGTR1) genes, have failed to consistently identify an association with migraine. We aimed at investigating the association between the 1166A>C polymorphism in the AGTR1 gene in several primary headaches.

Methods: The 1166A>C polymorphism in the AGTR1 gene was determined in DNA isolated from whole EDTA-blood from patients with primary headaches in addition to healthy, non-migrainous controls, using LightCycler primer and probe technology (Roche Diagnostics). Due to relatively small samples, we used non-parametric tests and α = 0.001.

Results: There was no difference in genotype or allele frequency between a control group (n= 198) and a migraine group (n= 208), a migraine with aura subgroup (n= 80), a migraine without aura subgroup (n= 128), a cluster headache group (n= 94) or a group with tension-type headache (n= 32) respectively.

Conclusion: The distribution of genotypes and alleles in the AGTR1 gene were very similar to that of controls among all headache patients and in subgroups with migraine, cluster and tension-type headache. Hence this polymorphism does not seem to be important in the pathophysiology of these headaches.

PSI-219

A pharmacoepidemiological study of anti-migraine prescribing in South Africa

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Background and aims: Migraine affects primarily the young adult population and is responsible for many lost working days each year since it affects mostly the economically active sector of the community. The primary aim of the study was to determine the prescribing patterns of anti-migraine agents and to compare the results with previous South African studies.

Methods: A retrospective drug utilisation consumption study was conducted on 2009 data obtained from a medical aid administrator. The database contained 2292652 records (procedures, consultations and medication).
All medication records for anti-migraine agents were extracted and analysed.

**Results:** A total of 1463 products were prescribed to 752 patients at a cost of R178862. The average cost was R122.26 (SD = R109.69) per product. The average age of patients was 41.32 (SD = 14.56) years, with 69.55% of patients between 30 and 59 years of age. Two-thirds of patients (67.29%) were female. Patients were prescribed an average of 1.95 (SD = 2.04) products over the year (females 2.07 products, males 1.70 products). The Lorenz curve was used to illustrate skewness in prescribing. Clonidine was the most often prescribed active ingredient (56.05%), followed by rizatriptan (17.22%). The selective 5HT1-receptor agonists (triptans) accounted for 27.75% of prescriptions for anti-migraine agents, compared to 18.94% in 2008 and 25.50% in 2004. Prescribing patterns of triptans changed as new active ingredients became available on the market and their cost also fluctuated.

**Conclusion:** Studies on the pharmacoepidemiology of migraine will greatly enhance the understanding of this disease state in South Africa.

**PS1-220**

Reversible cerebral vasoconstriction in migraineurs

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**Background:** Reversible cerebral vasoconstriction syndrome in migraineurs should not be misdiagnosed because the risk of stroke may increase if they use triptans.

**Purpose:** Can migraineurs distinguish the headaches with cerebral vasoconstriction (CV) from migraine attacks?

**Objective and methods:** Migraineurs who visited our Headache Clinics and had been diagnosed as having reversible CV were recruited. MRA was repeated until CV improved. Their clinical characteristics and neuroimaging were assessed.

**Results:** Three migraineurs had reversible CV. Case1: A forty years-old female experienced recurrent severe headache attacks after Caesarean section. She visited our Clinic 10 days after the onset of unusual headaches. MRA revealed multiple CV. Case2: A forty-one years-old female experienced multiple thunderclap headaches for 5 days and visited our Clinic. CT revealed cortical subarachnoid hemorrhage, no aneurysm was detected but reversible CV was observed by MRA and angiography. Both patients were admitted to our hospital. After using intravenous nifedipine, blood pressure normalized and headaches improved. Case3: A forty years-old female visited our Clinic because it was the first time that her migraine headache last 3 days. MRA during headache attack revealed multiple CV, and her headache diminished after taking NSAIDs. In the repeated MRI, CV improved.

**Conclusions:** Reversible CV may be associated to the thunderclap headache and most migraineurs could distinguish the headaches with CV from migraine attacks. One of our patient showed CV during the similar headache attack with her usual migraine attacks. The pathogenesis of reversible CV may be multifactorial. Further clinical data are required to elucidate this intriguing conditions.

**PS1-221**

Normal pressure pseudotumor: a series of thirteen cases

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**Introduction:** Idiopathic intracranial hypertension (IIH) requires CSF pressures of >200mm H2O in non-obese patients and a CSF pressure of >250mm H2O in obese patients. Lower CSF pressures, however, may be sufficient to produce CDH which responds to treatment for IIH.

**Methods:** Thirteen patients with CDH underwent lumbar puncture (LP) and experienced headache improvement after CSF withdrawal despite normal OP. Their demographics and response to medical and/or surgical management were recorded.

**Results:** 23% were male (n=3) and 77% female (n=10). Mean age was 38.7 years (range 21-52) and mean BMI was 34.0 Kg/M^2^ (range 18.6-44.5). Mean OP was 182.3mm H2O (range 170-230) with 2 OPs >200 (both in obese patients). 92% (n=12) presented as chronic migraine. 7 patients underwent shunt placement (6 ventriculoperitoneal and 1 lumbo-peritoneal) 6 of which (86%) improved significantly. Of these 6 patients, 5 noted sustained benefit and one developed a peri-operative subdural hemorrhage requiring shunt removal. Of the 6 patients that were not shunted, 1 noted significant and sustained improvement on acetazolamide while the remainder have responded poorly to medical management and are being considered for shunt.
Conclusions: IIH is underrecognized based on current criteria. Some patients with normal OP and CDH may improve after CSF withdrawal because:

- CSF pressure thresholds are individualized and headache may occur with normal OP.
- A spot-check OP is inadequate to diagnose IIH as CSF pressure may fluctuate.

Patients with refractory CDH should undergo LP and IIH should be considered in patients with a positive response to CSF withdrawal.

PS1-222

Acute allodynia in migraine patients and its association with medication overuse

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Objective: To determine the presence of cutaneous allodynia in migraine patients in a secondary Headache Center and assess its association with specific headache characteristics and comorbid disorders.

Background: Allodynia, pain resulting from application of a non-noxious stimulus, is a described symptom of migraine, especially of chronic migraine, with a potential role in directing optimal treatment for migraine attacks.

Methods: A total of 573 consecutive patients presenting at a Headache Center of Spedali Civili of Brescia were enrolled to determine the presence of acute cutaneous allodynia. We showed the data of migraine patients (N = 408), excluding patients with migraine with aura (N = 15) and other kind of headache.

Results: We divided the patients into: migraine without aura (N = 349), of these 66 with medication-overuse, chronic migraine (N = 59), of these 33 with medication overuse according to the revised ICHD diagnostic criteria. Acute allodynia was present in 145 (35.5%) and allodynia was significantly more often present in patients with medication overuse (45.5%) than in patients without medication overuse (32.5% p < 0.05). On the contrary there was no correlations between allodynia and variables such as headache frequency or other risk factors of migraine chronification.

Discussion: Our findings suggest that allodynia could be a marker for a more severe migraine disorder. An underlying implication is that central sensitization, in subjects with an altered regulation of the central nociceptive pathway, as migraine subjects, could predispose to development of medication overuse. Different pathogenetic mechanisms may play a role to development of acute allodynia and additional studies are required.

PS1-223

Pharmacokinetics of the CGRP-receptor antagonist bi44370 during and between migraine attacks

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Objectives: Primary objective targeted the relative oral bioavailability of BI44370 during a migraine attack compared to a migraine-free period. Secondary objectives included efficacy, safety and tolerability of BI44370 in acute migraine.

Methods: Open-label, fixed-sequence, two-period trial with intraindividual comparison of one single oral dose of BI44370 (200mg) during a migraine attack and one dose during the migraine-free period.

Results: Nineteen migraine patients (12 women, 7 men) participated; sixteen were evaluable for pharmacokinetic analysis. During migraine headache, the pharmacokinetics of BI44370 showed higher interindividual variability compared with the migraine-free period. The lag time (tlag) of BI44370 was delayed by 15min and tmax was prolonged by 0.5h compared with the migraine-free period. Cmax was achieved within 1h in 14 patients (87.5%) when given during a migraine-free period versus 11 (61.1%) during migraine headache. AUC0-2 was reduced by 45% (90%CI 15-64%) during the migraine attack. The reductions of Cmax (24%) and AUC0-\infty (16%) were not statistically significant. Terminal elimination half-life was not affected. The intra-individual variability of the pharmacokinetic parameters was very high (gCV 46.7%-78.1%). Pain-relief at 2 h after dosing of BI44370 was reported by 12 patients (63.2%). Sustained pain-relief response (i.e. up to 24 h) was satisfying in 11 patients (57.9%). No serious adverse events occurred. No adverse events led to discontinuation. No changes in vital signs (blood pressure and pulse rate) or ECG were observed.

Conclusions: During a migraine attack, initial absorption of BI44370 is delayed and reduced. Overall absorption is not meaningfully affected. BI44370 is safe and well tolerated.
PS1-224
Pharmacogenetics of migraine: impact of serotonin transporter polymorphisms and haplotypes on triptan response

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Background and aims: Up to 40% of migraine patients do not respond adequately to triptan treatment. In the present study, we assessed the value of four polymorphic variants of the serotonin transporter gene (rs140701G and rs1042173T) as predictive factors for triptan response.

Methods: 130 Caucasian migraine outpatients of the Novara and Pavia Headache Centers were enrolled. In the first visit, patients were prescribed with one of six triptans available in Italy and given a headache diary. After obtaining the informed consent, a peripheral venous blood sample was taken. In the second visit the responsiveness to triptan was assessed (endpoint: 2 hours headache response). Statistic analysis was performed with a logistic regression model adjusted for age, gender, migraine-type diagnosis, triptan and prophylactic treatment. The threshold of significance required by Bonferroni correction was 0.0083 [P= 0.05/6 (4 polymorphisms + 2 haplotypes)].

Results: Patients homozygous for rs140701A, rs1042173G and STin2.12 alleles were found at lower odds of responding to triptans compared to carriers of the respective wild-type allele, whereas 5HTTLPR alleles were not associated with triptan response. The haplotype analysis showed that migrainous patient with STin2.10/STin2.12 haplotype had higher odds of achieving response to triptans compared to those with STin2.12/STin2.10 haplotype (OR: 3.79, 95% CI: 1.58-9.09, P=0.0034).

Conclusions: Our study is the first to have examined and shown that polymorphisms in the gene encoding the serotonin transporter, as single markers or in haplotype combination, affect the clinical response to triptans in migraine patients.

PS1-225
Comparisons of disability, hrqol and resource use between chronic and episodic migraineurs: a headache clinic study

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Background and aims: Chronic migraine (CM) is a disabling condition affecting 1.5% of the population. Patients with CM have a diagnosis of migraine and headache ≥15 days per month for ≥3 months; whereas, patients with episodic migraine (EM) have headache <15 days per month. We investigated if migraine status predicted disability, health-related quality of life (HRQoL) and health care resource utilization.

Methods: This study recruited patients with EM and CM in the headache clinic at the Veterans General Hospital, Taipei, Taiwan. Diagnosis was made by physicians based on patient interview. Participants completed a questionnaire including sociodemographics, Migraine Disability Assessment (MIDAS), EQ-5D, Migraine-Specific Quality of Life v2.1 (MSQ), Patient Health Questionnaire-4 (PHQ-4) and health care resource utilization.

Results: A total of 174 patients (143F/31M, mean age 42±11 years old) completed the study. Ninety-three patients had EM (53%) and 81, CM (47%). Age, gender and education levels did not differ between these two groups. CM patients reported significantly greater disability, lower HRQoL and greater health care resource utilization.

Conclusion: Compared to EM, CM was significantly associated with higher disability, lower HRQoL and greater health care resource utilization.
PS1-226

Accoustic mismatch negativity in medication-overuse and chronic tension-type headaches

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Objective: Medication-overuse Headache (MOH) is a kind of chronic disorder associating with analgesic abuse. Electroencephalographic differences among MOH, other types of headache patients and healthy people can provide evidence of pathophysiological changes in MOH. The mismatch negativity (MMN) of the event-related potentials provides an objective marker of involuntary stimulus selective processing, and helps investigate a possible neural mechanism of MOH. Thus, we hypothesize that MMN latency and amplitude might be dysmorphed in MOH.

Methods: We investigated MMN by an acoustic frequency deviance paradigm in 23 MOH, 21 chronic tension-type headache (CTH) patients and 40 healthy volunteers. Meanwhile, Self-rating Anxiety Scale and Self-rating Depression Scale were used to measure the degree of anxiety and depression.

Results: There was no significant difference for either N1 latencies/amplitudes to both standard and deviant stimuli among all groups, or MMN amplitudes between MOH and CTH. In MOH, MMN latencies at Fz, Cz and Pz were shorter than those in the other two groups, and its amplitudes at the three electrodes were lower than those in the healthy group. Besides, MMN latency was negatively correlated to the pain duration (with analgesic abuse) only in MOH.

Conclusion: The MMN abnormalities indicate a rapid but weak preattention in MOH, and the process of central sensitization might be facilitated by the suppression of the endogenous pain control system.

PS1-227

The safety and efficacy of occipital nerve stimulation for the management of chronic migraine


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Introduction: Chronic migraine is a debilitating disorder with few treatment options. Occipital nerve stimulation (ONS) is emerging as a potentially promising therapy for chronic migraine patients. We conducted a clinical trial to assess safety and efficacy of ONS for the management of headache pain and disability associated with chronic migraine.

Methods: In this prospective, multi-center, double-blind, controlled study, patients were implanted with a neurostimulation system (St. Jude Medical Neuromodulation) and randomized to an Active or Control group for 12 weeks. Patients then continued in an open-label phase with 24, 48, and 52 week evaluations. Scores for MIDAS, Zung Pain and Distress Scale (PAD), VAS, quality of life (QoL), satisfaction, and adverse events were reported.

Results: Most patients (153/157) completed the 12-week visit. There were significant group differences for all assessments at 12 weeks (p < 0.01). In the Active and Control groups respectively, MIDAS headache days decreased by 22.5 and 3.4, total MIDAS scores improved by 64.6 and 20.4, PAD scores improved by 13.3 and 5.5, VAS scores decreased by 14.1 and 7.0, 35.2% and 11.5% of patients achieved a 30% reduction in VAS, 66.7% and 17.2% of patients reported improved QoL, and 51.4% and 19.2% were satisfied. Overall, the rate of serious device- or procedure-related events was 1.0%. These events included 1 case of infection and 1 case of expected post-operative pain that required hospitalization.

Conclusion: The results provide evidence to support safety and effectiveness of ONS for the management of headache pain and disability associated with chronic migraine.
Domperidone does not abort migraine at the prodromal stage

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Prodromal symptoms are common in migraine, occurring in approximately 20% of sufferers for hours to days before the onset of headache. Common prodromal symptoms include fatigue, yawning, neck pain, and excessive urination, and are thought to be mediated by cerebral dopaminergic systems.

Waelkens’ studies, published in the mid-1980s, suggested that domperidone, a dopamine agonist not thought to cross the blood-brain barrier in significant quantities, could prevent migraine attacks if taken in the prodromal phase. No subsequent studies of this nature have ever been published.

A pilot study was undertaken to assess whether Waelkens’ findings could be replicated. Patients reporting prodromal symptoms were asked to take oral domperidone 20 mg at the onset of symptoms, continuing 8 hourly until headache onset, or for three days if no headache developed.

15 patients (3M, 12F) with prodromal symptoms (duration 2-48 hours) took domperidone in this way for at least three attacks. Of these, 14 patients reported no effect whatsoever from doing so, with headache developing in the normal manner at the usual time. Just 1 patient reported a possible reduction in the severity of his attacks, and continued to use domperidone beyond the initial trial of three attacks.

Domperidone has therefore not been shown to possess any significant efficacy in aborting migraine attacks at the prodromal stage. Further pilot studies, using medications with better CNS penetration, might provide more encouraging results.

The icon study: occipital nerve stimulation in medically intractable chronic cluster headache design and protocol

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Introduction Recent pilot studies suggest that occipital nerve stimulation (ONS) in medically intractable chronic cluster headache (MICCH) might be an effective treatment. There are no randomised clinical trials and a placebo effect cannot be excluded due to paresthesias when active.

Objective Here we propose a prospective, randomised, double blind, parallel group multi-centre international clinical study to compare the reduction in attack frequency from baseline induced by ONS, in patients with MICCH between two different stimulation conditions: high (100%) and low (30%) intensity stimulation.

Methods Following implantation there will first be a run-in phase of 10 days of 10% stimulation intensity, followed by a stepwise monthly increase up to either 30% or 100%. Patients will be assessed monthly by a blinded assessor. The primary outcome measure is the mean number of attacks over the last 4 weeks of the double blind 6 month treatment period in the 100% versus the 30% treatment group. A repeated measures analysis of variance will be used to evaluate a stimulation effect over time and a dose response effect. Hereafter, in an open extension phase of 6 months, all patients will receive 100% stimulation or the stimulation considered optimal by the patient. Secondary outcome measures include the rate of responders (≥ 50% reduction in attack frequency), medication use, quality of life, mean pain intensity, economic evaluation and whether patients would recommend the treatment to another patient. We will also investigate whether predictive factors can be identified for efficacy.

Results The trial is currently ongoing.

Superior vena cava blood cgrp levels, but not antecubital blood levels, correlate with symptoms during the treatment of chronic migraine

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Introduction Recent pilot studies suggest that occipital nerve stimulation (ONS) in medically intractable chronic cluster headache (MICCH) might be an effective treatment. There are no randomised clinical trials and a placebo effect cannot be excluded due to paresthesias when active.

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Results The trial is currently ongoing.
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**Background:** Studies measuring CGRP in external jugular and antecubital blood during migraine have had conflicting results. Little is known about CGRP levels in chronic migraine.

**Methods:** 15 patients admitted to an inpatient service for the treatment of chronic migraine and scheduled to receive a PICC line (peripherally inserted central catheter) were selected. Subjects were excluded if they had psoriasis, took an ACE inhibitor or an ARB, or used triptans within 24 hours or DHE within 48 hours of admission. PICC samples were collected three times daily and peripheral samples once daily. Symptom status was recorded at the time of each sampling.

**Results:** There were 14 females. Age was 41.5±10.6 years. Severity on admission was 5.0±2.2 out of 10 and on discharge 1.5±1.4. Length of stay was 6.9±2.5 days. CGRP values from PICC and peripheral blood were correlated with an r value of 0.76 (p<0.001). Mixed models were used to detect multivariate associations with CGRP levels. Peripheral CGRP was not associated with headache intensity, sample time, throbbing pain, photophobia or phonophobia. PICC CGRP was associated negatively with duration of hospital stay (p=0.008) and positively with severity of phonophobia (p=0.02).

**Conclusions:** PICC CGRP levels decreased over the course of each patient’s hospital stay. However, the lack of other supporting correlations suggests a more complex role for CGRP involving factors not considered in this study. Peripheral CGRP levels appear to not correlate with symptoms. More work must be done to further our understanding of the role of this peptide in migraine pain.

**PSI-231**

**IN VITRO characterization of a group of potent and selective human monoclonal antibodies against cgrp receptor**

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The efficacy and safety of current migraine medications leave room for improved therapies. Clinical studies have demonstrated that CGRP receptor antagonism is an effective approach to treat acute migraine pain. After the successful generation of a group of CGRP receptor antagonist peptides and PEGylated antagonist peptides, we now have generated multiple human monoclonal antibodies (MAb) that specifically target the human CGRP receptor.

Our CGRP receptor antibodies have demonstrated as low as pM binding potency (Kl) in radio-ligand binding competition assays using membranes from SK-N-MC cells which endogenously express human CGRP receptor. In cell-based functional assays, the MAbs inhibited CGRP-stimulated cAMP production with IC50s between 1 to 20 nM. While being highly selective to human CGRP receptor, these antibodies had minimum activity at the rat receptor and demonstrated > 50-fold selectivity over other closely related receptors in the family. Biacore binding competition analysis indicated that all tested MAbs recognize the same or very similar and strongly overlapping epitope(s). The newly generated anti-CGRP receptor antibodies have shown to be a significant improvement over the previously reported anti-CGRP receptor peptide antagonists.

**PSI-232**

**Higher degree of atherosclerosis is associated with lower prevalence of migraine in aged people**

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**Background:** The prevalence of migraine gradually decreases with advancing age. We investigated whether increasing degree of atherosclerosis and vascular changes contribute to the lower prevalence of migraine in aged people.

**Methods:** Among 49 patients aged over 50 years who had been diagnosed with migraine, 30 who had been responsive to triptan were assigned to the migraine group, while 19 who had been poorly responsive to triptan, but no longer had migraine at the time of this study were assigned to the control group. We examined the degree of atherosclerosis using non-invasive measurements, i.e., ankle brachial pressure index (ABI), brachial ankle pulse wave velocity (baPWV), cardio ankle vascular index (CAVI), and intima-media thickness (IMT), in both groups.
**Results:** There was no difference in age or ABI between the two groups. baPWV in the migraine group was significantly slower than that in the control group \((p < 0.05)\). CAVI showed a normal pattern in 86% of patients in the migraine group, but in only 46% in the control. Concerning cervical atherosclerotic findings, the incidences of patients with less than 1 mm IMT in the migraine and control groups were 83% and 50%, respectively. In migraine patients aged over 60 years, 78% showed less than 1.1 mm IMT, whereas 56% of control patients over 60 showed more than 1.2 mm IMT.

**Conclusion:** The degree of atherosclerosis is significantly less in aged migraine patients than in controls. Non-invasive evaluation of atherosclerosis could be useful as an indication for triptan treatment in aged migraine patients.

**PS1-233**

An open-label study to evaluate the long-term safety of zelrix™, a sumatriptan iontophoretic patch for the treatment of acute migraine

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**Background/aims:** The Zelrix™ (NuPathe, Inc., Conshohocken, PA, USA) patch uses proprietary iontophoretic technology to deliver sumatriptan transdermally. In a previous phase III study (NP101-007), Zelrix was superior to placebo for the treatment of migraine symptoms, demonstrating pain relief as early as 1 hour following treatment. The current study evaluated the long-term safety of treatment with Zelrix.

**Methods:** This phase III, open-label extension study enrolled patients previously treated with Zelrix in NP101-007. Patients received ≤6 Zelrix treatments during any 30-day period and were treated for ≤12 months. Adverse events (AEs) were monitored throughout the study; electrocardiograms were performed at enrollment \((t > 30 \text{ d from final visit of NP101-007})\), month 6, and month 12/ final visit; and vital signs were evaluated at all visits except patch-dispensing visits.

**Results:** One-hundred seven (58%) of the 183 patients in the safety population experienced ≥1 treatment-emergent AE over the course of the study, with most classified as mild or moderate. Application site conditions were the most frequently reported AEs (45%). Twenty-five patients (14%) discontinued owing to AEs, mostly application site conditions (23 patients). The incidence of triptan-related AEs was low (2%). No increase in AE incidence occurred with continued use. One patient experienced a nonspecific, not clinically significant electrocardiogram abnormality considered possibly related to study drug. No increase in skin irritation occurred with successive use. Eleven patients (6.0%) reported allergic contact dermatitis, which led to the discontinuation of 9 of these patients.

**Conclusions:** There was no overall decrease in tolerability and safety over the 12-month study.

**PS1-234**

The effect of ghrelin on cortical spreading depression in the rat

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**Objectives:** In the present study, we investigated the influence of ghrelin on the cortical spreading depression (CSD) induced in the rat.

**Methods:** Six male Sprague-Dawley rats \((330-400\text{g})\) were anesthetized with \(\alpha\)-chloralose and urethane, intubated, and ventilated mechanically. Blood pressure and other physiological parameters were monitored. For measurement of CBF (laser-Doppler flowmetry) and DC-potential (by platinum electrode), 2 burr holes were made at the parietal bone. Also, the right femoral vein was cannulated for intravenous administration of ghrelin. CSD was induced by dropping 3µl of 1M KCl on another posterior burr hole.

**Study protocol:** At first, the change of DC-potential and CBF (during induced CSD) were measured continuously after dropping 1M KCl for an hour. Then, 2 µl of 100pM of ghrelin in saline was injected. After that CSD was immediately induced and continuously monitored CBF and DC potential for another hour.

**Results:** There was a significant decrease in the frequency of CSD after the injection of ghrelin compared with pre injection. But there was no difference in the mean change of CBF value of post injection compared with pre injection. Also there was no difference in DC potential after ghrelin injection.

**Conclusions:** Our study suggested that ghrelin decreases the frequency of CSD. It was suggested that ghrelin may have some influence on the pathogenetic mechanism of migraine.
PSI-235

Sleep in children with migraine and tension type headache: preliminary study

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Background and aims: Clinical studies performed in adult populations indicate that certain headache types may be related to specific sleep stages, but there is a lack of research examining the relationship between headache and sleep in children. The aim of the study was to evaluate sleep in children with migraine (MH) and tension type headache (TTH).

Methods: 450 children and adolescents with headache (16% MH vs. 84% TTH) seen in the neurology clinic in 2 year were screening for sleep problems. Parents completed the sleep and headache questionnaire. Thirty one (20 MH and 11 TTH) agreed to undergo nocturnal polysomnography.

Results: The parents of children with MH reported more frequent day-time naps: 37% vs. 24.4% in TTH (p = 0.026); daytime sleepiness 26% vs. 11.7% (p = 0.001); learning difficulties 30.1% vs. 19.6% (p = 0.045). Snoring was reported more frequently in children with TTH (24.9%) than in MH (13.7%) (p = 0.037). On polysomnography, sleep latency was significantly longer in MH (19.2 min) than in TTH (11.6 min) (p = 0.048), N2 latency was longer in MH too (p = 0.028). The REM sleep latency was significantly shorter in MH (100.4 min) than in TTH (153.2 min) (p = 0.01). MH had a mean of 5 REM periods vs. 4 periods in TTH. In Fast Fourier Transformation, theta power in REM sleep was significantly higher in MH than in TTH.

Conclusion: It is necessary to conduct further research on a larger group in order to better correlate the prevalence of sleep disorder symptoms with the type of primary headache and daytime functioning.

PSI-236

A family with a new notch3 mutation for casadil (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) disease

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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare inherited cerebrovascular disease frequently associated with mutations in the Notch3 receptor, localized in chromosome 19. Its main clinical manifestations are recurrent subcortical ischemic infarcts, subcortical dementia and migraine headaches. We describe three members of a family (cases are brother, sister and cousin) with a clinical-neuroimaging picture of CADASIL who showed a previously undescribed Notch3 mutation.

Material and methods: Three members of the same family with a clinical-neuroimaging picture of CADASIL underwent clinical, radiological, laboratory and genetic characterization studies. The studied subjects were two sisters and their brother. The associated Notch3 mutation was further evaluated by site-directed mutagenesis.

Results: CADASIL was caused by a novel Notch3 missense mutation C.2444t>c (pcys82Arg) in the three members of the studied family. All of them suffered the typical clinical pattern of migraine headaches, recurrent subcortical infarcts and subcortical dementia. The man also suffered from diabetes mellitus and one sister also had dyslipidemia. Cerebral lesions (studied by magnetic resonance imaging) showed both demyelinating and typical CADASIL topography, including peri- and paraventricular white matter lesions.

Conclusions: Although the CADASIL clinical-neuroimaging picture has been well defined, there is increasing evidence for new Notch3 (and other genes) mutations that could cause this genetic disorder. A better understanding of these mutations is vital to comprehend the pathophysiology of this disease and the role of Notch3 in vascular tissue.

PSI-237

Nitric oxide modulates hmgbl and hif expression in pmbs of migraine without aura and cluster headache patients

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Background and aims: Migraine represents one of the most prevalent and disabling headache disorders, but the mechanisms underlying its pathophysiology are still
unknown. Many studies reported that an immunological disequilibrium, a sterile inflammatory status, an abnormal presence of NO in the trigeminal-vascular circulation, are strictly related to migraine attacks.

Knowing that cytokines play an important role in several physiological and pathological settings, we analyzed the expression of two new described cytokines, HIF and HMGB1, on PMBCs of MwoA (n=10) and CH (n=8) patients. We also studied the effects played by NO on the expression and the release of both this biological mediators.

**Methods:** Mononuclear cells were obtained by patient peripheral blood samples using a Lymphoprep gradient. HIF and HMGB1 expression on PMBCs have been analyzed by Western Blot analysis. NO was detected in cell incubation supernatants using the Griess reagent.

**Results:** Our results demonstrated the expression of HIF and HMGB1 in PMBCs of MwoA and CH patients suggesting a real involvement of both these cytokines in headache pathogenesis. We also showed the ability of NO to modulate HIF and HMGB1 expression.

**Conclusions:** Data obtained revealed that HIF and HMGB1 may be involved in the pathogenesis of migraine attacks even if at different extent: in fact we postulate that MwoA pathogenesis is related to a proinflammatory state, whereas in CH is involved a hypoxic condition. Therefore the pharmacological modulation of the expression of both HIF and HMGB1 could be considered in the next future for therapeutic effects.

**PS1-238**

**7 tesla 1H-MRS changes in the cerebellum of hemiplegic migraine patients; report from lumina**

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**Background:** Hemiplegic migraine is a rare subtype of migraine, characterized by hemiparesis during the aura phase. Genetic studies have identified several mutations leading to Familial Hemiplegic Migraine (FHM), a monogenic subtype of hemiplegic migraine. The aim of this study was to investigate regional biochemical changes with 7 Tesla ¹H-MRS in the brains of hemiplegic migraine patients.

**Methods:** Eighteen patients with hemiplegic migraine (M:F, 7:11; age 38.1 ±14.4 years) of which seven had a known FHM mutation (five CACNA1A and two ATP1A2) and 20 healthy control subjects (M:F, 7:13; age 35.7 ± 16.8 years) were studied. We used single-voxel 7 Tesla ¹H-MRS (STEAM, TR/TE=2000/19/21ms) to interictally investigate four different brain regions: hypothalamus, occipital lobe, pons and cerebellum. Concentrations of alanine, choline, creatine (Cre), GABA, glutamine, glutamate, lactate, myo-inositol, N-acetylaspartate (NAA), N-acetylaspartylglutamate, scyllo-inositol, and taurine were estimated using LCModel fits. Metabolite ratios (relative to Cre) were statistically compared.

**Results:** In the cerebellum total NAA/Cre ratio was lower in hemiplegic migraine patients (0.740, SD 0.101) versus healthy controls (0.799, SD 0.079; p < 0.05). No differences were found for other metabolites or regions.

**Conclusions:** This is the first time high resolution 7 Tesla ¹H-MRS spectra were used to investigate interictal biochemical changes in the brains of familial and sporadic hemiplegic migraine patients. The lower tNAA/Cr ratio in the cerebellum of hemiplegic migraine patients indicates neuronal loss or dysfunction.

**PS2-1**

**Psychopathologies in migraine and tension headache**

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Headache represents one of the most frequent human discomforts, its significance is often abstruse for it may signal serious disease or represent only tension or fatigue and present a persistent and significant clinical challenge, research shows that psychotherapeutic results are not always maintained and pain is unrelieved. The objective of the research was to find the underlying psychopathologies which are causing, maintaining and exacerbating headaches. After an initial pilot study on 19 patients this was carried out in two phases, in phase a 100 headache sufferers, age range 15-55 diagnosed with Migraine/Tension Headaches were recruited. All under-went diagnostic clinical examination by the Psychiatrist, and only those who fulfilled the criteria of the (Ad hoc Committee for the Classification of the headaches (1962) were referred to the Clinical Psychologist for psychological assessment. Crown and Crisp Experiential
Index, adapted version, Afaq & Najam (1992) clinically used in hospitals was utilized to assess psychological status, it has six sub scales: Depression, Free floating anxiety, phobia, somatic, obsession and Hysteria. Significantly higher levels of depressive psychopathology were found in headache patients. These subjects also scored higher on free floating anxiety, Hysteria and very high on somatic scales, keeping in view the above findings phase b a longitudinal study of 37 patients with chronic (reported) headaches was carried out using CCEI, the findings in both studies shed light to help headache patients and the clinicians to achieve effective management of headaches.

**PS2-2**

**Headache: efficacy of effective management techniques**

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Pain is one of the greatest of human experiences and headaches present a significant clinical challenge. Headache treatments are diverse ranging from Trephining of the skull wearing of head bands, Injeestion of herbs to Imagery, Bio Feedback, Relaxation Training, Placebo, Hypnosis, Diaphragmatic Breathing, Imagery, Acupuncture, Acupressure, Cognitive Behavior Therapy, Radio frequency, New Wave Neuro Technology, Neurotomy, Transcutaneous Electrical Nerves Stimulation, Trigger-point Injections, Botox, Cryoneurolysis, Pharmacotherapy, Therapeutic Touch, Hyperbaric Oxygen Therapy, Preemptive Analgesia, Ozone Therapy, Water Cure, Herbal Medicines, Aroma Therapy, Rolfing, Botulinum Toxins, Healing scents, B Vitamins, Music, Caffeine, Omega 3 and Prayer.

**Objectives:** To compare the efficacy of various modalities of headache treatment.

**Method:** Headaches sufferers (N=37) ages range 15-55 diagnosed with Migraine/Tension and Combined headaches recruited from hospitals, underwent diagnostic clinical examination. Those who met criteria (Ad hoc Committee for the Classification of Headaches 1962) were referred to the clinical psychologist for assessment and treatment. Pre and post assessments using Interview, MPQ, Faces test, Rating scales, medication index and subjective report of pain were carried out. All participants underwent six weeks of intervention in their respective groups a Drugs, Drugs plus Psychotherapy, Acupuncture Relaxation, Training and Placebo. Significant differences were found among treatment groups, findings of the study showed that Drug plus Psychotherapy is superior to other interventions, but other modalities like Acupuncture, Relaxation and Placebo have beneficial results on outcome.

**Conclusion:** These findings have important implications for future interventions. It is highly recommended that different modalities need to be integrated under one umbrella.

**PS2-3**

**Headaches in adolescents in bashkortostan, russia: comparing schoolchildren and university students**

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Headaches are an essential problem for adolescents, the recent systematic review (Abu-Arafeh I, et al, 2010) reports its prevalence as 58.4%, more often in girls (odds ratio = 1.5). Differences are observed in different countries, but data about headaches in adolescents in Russia are missing.

The aim of our study was to compare prevalence and characteristics of headaches in schoolchildren and young university students. We used questionnaires that distributed to 106 schoolchildren in a rural area (11-16 years of age) and 362 university students (17-24 years) in Ufa (mean age 18.8, SD=1.1). It was the first anonymous self-reported survey in Bashkortostan Republic, Russia.

The results showed high prevalence of headaches: just 16.0% of schoolchildren and 30.1% of students did not suffer from headaches. Headaches were more frequent in females (odds ratio = 1.2). Most of the schoolchildren mentioned headaches in the temporal part (34.8%), but most of the students had frontal headaches (62.4% vs. 22.5% in schoolchildren). Headaches intensity was more severe in students (45% of students and 21% of schoolchildren reported headaches of more than 7/10). Most of the schoolchildren with headaches (90.9%) had to take painkillers. Students seem to tolerate headache better: although 69.9% of all students reported headaches at the moment of the study, 69.3% of all students replied that they feel comfortable at the moment. The majority answered positively for the question about headaches in their parent (88.8% of schoolchildren and 58.8% of students).

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PS2-4

Frovatriptan vs. Zolmitriptan in the acute treatment of menstrually-related migraine: analysis of a double-blind, randomized, multicenter, comparative study

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Objective: To compare the efficacy and safety of frovatriptan and zolmitriptan in the specific treatment of menstrually related migraine (MRM), analyzing data from a multicenter, randomized, double blind, cross-over study.

Methods: We analyzed the subset of 76 normally menstruating women who participated in one head-to-head multicenter, randomized, double blind, cross-over clinical trial and who took the study drugs to treat MRM attacks. Each patient received frovatriptan 2.5 mg or zolmitriptan 2.5 mg in a randomized sequence: after treating 3 episodes of migraine in no more than 3 months with the first treatment, the patient had to switch to the other treatment. MRM was defined according to the criteria listed in the Appendix of the last IHS Classification of Headache disorders.

Results: A total of 73 attacks classified as MRM were treated with frovatriptan and 65 with zolmitriptan. Rate of pain relief at 2 hours was 52% for frovatriptan and 53% for zolmitriptan (p=NS), while rate of pain free at 2 hours was 22% and 26% (p=NS), respectively. At 24 hours, 74% and 83% of frovatriptan-treated and 69% and 82% of zolmitriptan-treated patients were pain free and had pain relief, respectively (p=NS). Recurrence at 24 hours was significantly (p<0.05) lower with frovatriptan (15% vs. 22% zolmitriptan).

Conclusions: Frovatriptan proved to be effective in the immediate treatment of MRM attacks, similarly to zolmitriptan, but showed significantly lower recurrence rates, and thus a better sustained relief.

PS2-5

Importance of the initial headache of subarachnoid hemorrhage in the patients with the age of 80 years and older from a single center analysis


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Background: In the developed countries, especially Japan, elderly population is rapidly increasing, but outcomes of elderly patients with the age of 80 years and older suffering from subarachnoid hemorrhage (SAH) remain still unclear.

Methods: We retrospectively reviewed the medical records of non-traumatic SAH patients aged 80 years and older, who were hospitalized in a single center between 1998 and 2009.

Results: There were 28 patients (80-90 years old and 75% female), representing 5.9% of all non-traumatic SAHs (n = 474). Median length of admission time from the first symptom of headache was 0 day (25th-75th percentile: 0-3 days; range: 0-26). Of those, 16 patients received an intervention (ten clipping and six endovascular coiling) and the remaining 12 patients were managed conservatively. The median survival time of intervention group was 110 days and that of conservative group 49 days (p = 0.12, log rank analysis). Cox’s proportional hazards model yielded two variables, the Japan Coma Scale (JCS) grade on admission (hazard ratio: 2.93 [p = 0.009]) and conservative treatment (hazard ratio: 2.14 [p = 0.054]). In the outcome of the Modified Rankin Scale, the shorter time form the first headache to admission (p = 0.0048) and the good admission neurological status (p = 0.031) may have the good outcome by logistic regression analysis.

Conclusion: In the elderly patients with good initial clinical condition, an acute intervention, and the recognition of the importance of initial headache may have good outcome.

PS2-6

Association of neck pain with reduced physical quality of life, increased neuroticism and mental vulnerability scores adjusted for comorbid headache: a cross-sectional population study

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Background and aims: Neck pain is comorbid with primary headaches including migraine and tension-type headache and may influence patient-reported outcomes. We aimed to assess the association of neck pain with mental vulnerability, depression, neuroticism and health related quality of life (HRQoL) in a population sample of persons with or without primary headache.

Methods: A community sample of 524 subjects completed a headache questionnaire and provided data on neck pain, mental vulnerability (12-item Mental Vulnerability Scale), depression (Major Depression Inventory), neurotic personality traits (EPQ), and mental and physical HRQoL (SF-12).

Results: Subjects with neck pain were 4 times more likely to have primary headache (OR=4.12; 95%CI: 2.62-6.48, p<0.001), higher mental vulnerability scores (1.98 vs. 1.12, p<0.001), higher depression scores (6.38 vs. 4.42, p<0.001), higher neuroticism scores (7.85 vs. 5.80, p<0.001) and lower SF-12 scores for both mental health (52.19 vs. 53.45, p=0.004) and physical health (49.48 vs. 51.89, p=0.003). After adjusting for age, gender, and education, neck pain remained a predictor of mental vulnerability (p<0.001), depression (p=0.009), neuroticism (p<0.001) and physical SF-12 scores (p<0.001). After adding primary headache disorders to the model, neck pain remained a predictor of mental vulnerability, neuroticism and low physical SF-12 scores.

Conclusion: In the general population, after adjusting for demographic features and headache status neck pain was independently associated with higher mental vulnerability scores, depression scores, and neuroticism scores, and lower SF-12 scores for physical health. These findings suggest that the association of other factors with neck pain may be accounted for by comorbid primary headache.

PS2-7

Alice in wonderland syndrome (awls): migraine aura or migraine ‘flashbacks’?

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As the analysis of AWLS symptoms during and out of migraine (M) attack has never been performed, the aim of the study was to investigate AWLS manifestations occurring intra- and interictally.

Patients: 7 patients (F-6, M-1, m. age 23.3) with migraine with (MA) or without aura (MO) and AWLS were included in the study. Somatic, neurological and psychiatric state, MRI, EEG were normal in all cases. Special inventory was used to analyze AWLS.

Results: Age of M and AWLS onset was 11.4 and 13.6 years. M attack frequency was 5 per month to 1 per year, AWLS manifestation frequency - from 1 per week to 1 per year. In 4 patients AWLS was the symptom of M aura and could also occur interictally; in 3 patients AWLS manifestations occurred only out of M attacks. Patients with interictal AWLS were younger than those with interictal AWLS (16.5 and 32.3 y.o.). Most typical AWLS symptoms were disturbances/distortion of: body image (100%) - size (100%), shape (57.1%); derealization (100%); déjà vu (100%); time perception alterations (85.7%); visual illusions (100%) - macropsia (100%), micropsia (57.1%), teleopsia (85.7%); visual hallucinations (57.1%). Patients with hallucinations were younger than without hallucinations (14.8 and 34.7 y.o).

Conclusions: AWLS manifestations can occur both during and out of M attack. AWLS is more typical for adolescent patients as a part of aura of long duration and numerous interictal manifestations (visual hallucinations, illusions etc). Interictal AWLS symptoms not related to M attack occur in adult M patients and are short-lasting.
47.64) and 387 men (mean age: 47.51); Episodic tension-type headache (ETTH) with 1023 women (mean age: 46.14) and 348 men (mean age: 44.64).

Results: Median headache duration was longer in women than in men in MwA (p = 0.0066), MwoA (p < 0.001) and CTTH (p = 0.0188). Median headache frequency in the preceding month was higher in women than in men in ETTH (p < 0.0070). Median VAS was higher in women than in men in CTTH (p < 0.001) and ETTH (p = 0.0028). The frequency of nausea was significantly higher in women than in men in MwA (p = 0.044). In MwoA, throbbing headache quality and related features (nausea, photophobia, phonophobia) were more frequent in women than in men. In CTTH and ETTH, those related features were also prominent in women (p < 0.05).

Conclusion: This study revealed for the first time, that gender has an impact on headache symptomatology in primary headache disorders.

PS2-9
SUNCT syndrome attributed to varicella zoster virus meningoencephalitis
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Introduction: Short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT) is a rare trigeminal autonomic cephalalgia.

We report the first case of secondary SUNCT attributed to Varicella Zoster Virus (VZV) meningoencephalitis studied with autopsy.

Case description: A 71-year-old diabetic male, with no history of neurological disease developed a sudden severe stabbing right-sided orbital pain of approximately 20 s duration, associated with dacryorrhea, that occurred up to 20 attacks per day. On day 6 he became febrile with ataxia and complete right facial palsy. He underwent a cerebral MRI scan, with no evidence of abnormalities, and a lumbar puncture, showing mononuclear pleiocytosis, hyperproteinorrachia, and detection of VZV genome with PCR. He was treated with intravenous acyclovir, gabapentin, and paracetamol. Headache improved progressively (1-3 attacks per day). Two days after acyclovir discontinuation, the patient developed left hemiparesis and dysphonia. A second cerebral MRI revealed an ischemic right ponto-mesencephalic lesion and a right ponto-bulbar meningeal thickening. Antiplatelet treatment was started. The patient became drowsy and then died. Autopsy confirmed the presence of a multifocal limphocytic meningoencephalitis.

Conclusions: We hypothesize that the viral infection could have resulted in irritation/inflammation involving the trigeminal nuclei, thus triggering the trigemino-autonomic reflex.

PS2-10
Tension-type headache, anxiety and sleep disorders
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Introduction: Several comorbidities have been related to tension-type headache (TTH), including anxiety, depression, hypochondriasis, sleep disorders and feelings of inadequacy. The relationship between these morbidities and TTH is poorly understood and has not been well studied. The aim of this study is to analyze the relationship between anxiety, sleep disorder and TTH.

Material and methods: One hundred and seventy two consecutive patients meeting the IHS criteria for episodic or chronic TTH were enrolled in this study. Demographic data, previous headache prophylactic medications, headache severity (0-10 Analogical Visual Scale), frequency (days with headache per month) and use of acute medications were collected and analyzed. Anxiety was measured according to Hamilton Anxiety Rating Scale and sleep quality was assessed by the Pittsburgh Sleep Quality Index. These two scales were compared with headache severity, frequency and use of acute medications using the Pearson’s correlation coefficient. Level of significance was set at P < 0.05.

Results: A significant correlation was found between anxiety and headache severity (r = 0.89), frequency (r = 0.83) and use of acute medications (r = 0.71). It was also found between sleep quality and headache severity (r = 0.84), frequency (r = 0.79) and use of acute medications (r = 0.69).

Discussion: Our findings confirm that in TTH patients, anxiety and sleep disorders are frequent co-morbid entities. Their prevalence increases when headache is chronic, severe and with a high medication consumption. A careful screening for the presence of an underlying anxiety or sleep disorders should be part of the clinical evaluation in these patients.
PS2-11

Tension-type headache, sleep disorders and prophylaxis with pregabalin

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Introduction: Although some prophylactic medications have been proposed to treat tension-type headache (TTH) there are still many refractory patients and others are warranted. Pregabalin, originally proposed as an anti-epileptic drug, has demonstrated efficacy in several sleep disorders, such as insomnia, a TTH associated comorbidity. The aim of this study is to evaluate the efficacy and tolerability of pregabalin in the treatment of TTH and sleep disorders.

Material and methods: Sixty one patients meeting the IHS criteria for TTH were enrolled. Pregabalin was initiated at 25mg/d and increased at 150mg/d over the first month. Then, it was modified until 300mg/d, as tolerated. Number of headache attacks, headache severity, acute medication and sleep quality (Pittsburgh Sleep Quality Index) were calculated. Significance level was set at P< 0.05. These variables were assessed before and 2 and 6 months after pregabalin.

Results: Headache attacks per month were reduced from 12.7±3.3 before pregabalin to 7.2±3.4 after treatment initiation. Headache severity changed from 5.8±2.1 to 4.4±2.0, the use of acute medication from 9.7±4.4 to 6.6±4.1 and sleep quality from 10.3±3.7 to 7.1±2.8. The improvement in sleep quality was related to the number of attacks (r=0.81), headache severity (r=0.76) and use of acute medication (r=0.61). Three patients discontinued pregabalin due to side effects and four because of lack of efficacy.

Discussion: Pregabalin has efficacy in TTH and associated sleep disorders. According to our results, this drug may be a safe and effective agent in tension type headache prophylaxis. Double-blind studies are warranted to confirm these findings.

PS2-12

Persistent idiopathic facial pain: neuromuscular procedure and orthosis rehabilitation

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Persistent Idiopathic Facial Pain (PIFP) is a nosographic entity whose diagnostic difficulties make underestimated. We wanted to clarify the role of the neuromuscular stomatognathic system in its pathogenesis. The 21 patients selected (M:4; F:17, mean age 40±28 yrs) were under EMG to determine efficiency of the Masseter muscles (MM) and the Anterior Temporalis muscles (TA) during activity and at rest. Patients were also under kinesiography (CMS) to identify the physiological rest position of the mandible after TENS muscular deprogramming. These patients were rehabilitated with a custom-made mandibular neuromuscular orthosis to provisionally correct the discrepancies identified. The EMG mean values of the muscles at rest were significantly above the norm for all 4 muscles and were normalized after TENS session. All 21 patients needed a mandibular advancement and 19 also a correction in the frontal plane, both obtained with orthosis. Wearing the device patients reached also a significant increase in muscular strenght (LTA: +25.37; LMM: +59.40%, RMM: +40.80%, RTA: +30.27) and a decrease in asymmetry (-30.21% for TA and -55.81% for MM) during maximal clench. After 12 months of follow up clinical results show a net decrease in VAS pain score with a mean shift from 9.5±0.8 to 3.5±1.2 with an encouraging improvement of life quality. Instrumental, statistical and clinical results suggest an association between PIFP and craniomandibular function. According to this, we consider that all patients with PIFP should undergo a CMS-EMG examination ruled following Neuromuscular Jankelson’s protocol.

PS2-13

Recurrent headaches are more often associated with self-perceived functional disability in females

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Background and aims: Headaches are a common cause of disability in both men and women. The aim of this study was to assess whether gender differences among medical students are related to the recurrence of headaches and if there is a difference in the perception of functional impairment caused by such headaches according to the gender.
Methods: A structured questionnaire was applied to 285 randomly selected medical students registered at the Federal University of Santa Catarina, Brazil, including students from the first to the sixth year of medical school education. The questionnaire assessed the gender of participants, the occurrence of headache episodes more often than once a month and the self-perception of functional disability in everyday life activities associated with recurrent headaches. The criterion for statistical significance was $p < 0.05$ (two tailed chi-square test).

Results: Among the 285 students assessed, 119 were males and 166 were females. The recurrence of headaches more often than once a month was reported by 135 students - 58.4% of female ($n=97$) and 31.9% of male ($n=38$) students assessed ($p<0.0001$). Some degree of disability was reported by 117 students, 26.9% of males ($n=32$) and 51.2% of females ($n=85$) ($p<0.0001$).

Conclusion: Females are significantly more associated to both recurrent headaches more often than once a month and higher self-perception of disability related to headaches.

PS2-14
Daily sleep duration and recurrent headaches in medical students
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Background and aims: Both sleep disorders and headaches are common in the whole population and often coexist in the same individual. The aim of this study was to determine the association between daily sleep duration and recurrent headaches among medical students.

Methods: A structured questionnaire was applied to 285 randomly selected medical students registered at the Federal University of Santa Catarina, Brazil, including students from the first to the sixth year of medical school education. The questionnaire assessed the occurrence of headache episodes more often than once a month and the self-reported daily sleep duration. The significance of this association was tested by the Fisher exact test (a two-tailed p-value of 0.05 was regarded as statistically significant).

Results: Among the 285 students assessed 47.4% ($n=135$) reported headaches more often than once a month, of which 62.2% ($n=84$) reported an average of up to 6 hours of sleep in a 24-hour period, while 37.8% ($n=51$) reported a habitual daily sleep duration of more than 6 hours. Among participants without recurrent headaches more often than once a month (52.6%, $n=150$), 44% ($n=66$) reported sleeping up to 6 hours and 56% ($n=84$) reported sleeping more than 6 hours daily ($p=0.003$). Students who sleep no longer than 6 hours daily had a 2.1-fold odds (95% CI, 1.3 to 3.4) of experiencing headaches more often than once a month.

Conclusion: Daily sleep duration no longer than 6 hours a day is statistically significantly associated with recurrent headache episodes among medical students in this sample.

PS2-15
Tolosa hunt syndrome
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Tolosa Hunt syndrome consists of retro or unilateral periorbital pain associated with ophtalmoparesis of the III, IV or VI cranial nerves with pain relief after beginning corticotherapy. It is a diagnosis of exclusion.

The authors present the following clinical case: a 56 year old woman with hypertension, depressive syndrome, right facial nerve paralysis three years ago and left facial nerve paralysis two years ago. The patient was observed in the emergency room due to right periorbital and supracillary pain associated with ipsilateral diplopia and ptosis with four days of evolution. The neurological exam showed incomplete paralysis of the III right cranial nerve: ptosis, medial rectus palsy, left looking diplopia with pupil constriction and dilation preserved.

Magnetic resonance imaging identified asymmetric cavernous sinus, with right cavernous sinus signal enhancement after contrast, traducing an inflammatory process.

The blood and CSF tests were normal.

Treatment with 1mg/Kg/day of prednisolone was initiated with pain remission after 48 hours.

After six months the magnetic resonance imaging showed resolution of the inflammatory process.

After analytical and imagiological studies, the excellent response to the beginning of corticotherapy and exclusion of other differential diagnosis, Tolosa Hunt syndrome diagnosis was established.
PS2-16

Association between vitamin D and headache

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Background: Case reports and a single-center study suggest low vitamin D levels may be associated with headaches. Additionally, a relationship between headaches and increasing latitude (regions with less sunlight) has been shown. Observational and randomized controlled data are lacking.

Aim: To investigate the association between serum 25-Hydroxyvitamin D ("25(OH)D") level and headache prevalence in a population-based survey.

Methods: We performed a cross-sectional analysis comparing vitamin D levels between adults with and without self-reported severe headaches or migraines using the 2001-2004 National Health and Nutrition Examination Survey, which is representative of the non-institutionalized civilian U.S. population. We used logistic regression to investigate an association between 25(OH)D levels and severe headaches/migraines adjusting for socio-demographics and significant confounders.

Results: Among 4,675 participants, 22% report severe headaches/migraines. A significant interaction between 25(OH)D and age (p-interaction = 0.001) exists in relation to headaches, such that no associations are observed among participants >40y (p-trend = 0.16). However, among those < 40y, compared to having 25(OH)D levels >40 ng/ml (100 nmol/L), the adjusted odds ratio of headaches associated with 25(OH)D levels < 10 ng/ml (25 nmol/L) is 2.56 (95%CI 1.18-5.52, p = 0.02; p-trend = 0.004). Conversely, compared to having 25(OH)D levels < 10 ng/ml, having 25(OH)D levels >40 ng/ml is associated with lower odds of headaches (OR = 0.39, 95%CI 0.18-0.85, p = 0.01).

Conclusions: Our findings show low vitamin D levels are associated with headaches, while higher vitamin D levels may be protective. Future studies are needed to determine if supplementing vitamin D to normal range reduces headaches, particularly among those < 40y.

PS2-17

Association between red blood cell folate concentration and headache

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Background: Some evidence has suggested that folate (vitamin B9) levels may be associated with headache. Recent studies have shown linkages between homocysteine and several folate-related genes to migraine. Hyperhomocysteinemia has previously been associated with increased risk of cerebrovascular disease.

Aim: To investigate the association between red blood cell (RBC) folate concentration (a long term marker of folate status) and headache prevalence in a population based survey.

Methods: We performed a cross-sectional analysis comparing RBC folate concentrations with and without self-report of severe headaches/migraines using the 2001-2004 National Health and Nutrition Examination Survey, representative of the non-institutionalized civilian U.S. population. We used logistic regression to investigate an association between RBC folate concentration and severe headaches/migraines adjusting for sociodemographics and confounders.

Results: Among 4,616 participants, 22% reported severe headaches/migraines. An inverse association between RBC folate concentration and headaches/migraines was demonstrated (p for trend = 0.03) when confounders were included (adjusted for age, sex, race/ethnicity, education, self-reported health, vitamin B12 concentration, smoking status and seeing a mental health provider). Post-hoc analyses showed anti-epileptic drug use, alcohol intake, and obesity had no significant affect on the association between folate and headaches/migraines.

Conclusion: Our study is consistent with recent publications suggesting links between low folate levels and increased risk of headaches/migraines; this is consistent with a possible mechanism between the homocysteine/folate pathway. This is of interest as it may contribute to understanding underlying pathophysiology of why migraine is associated with increased risk for cerebrovascular disease.
PS2-18

“Let-down headache”: reductions in stress and improvement in mood predict headaches in persons with migraine

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Background and aims: Relaxation after stress is hypothesized to increase the probability of headache in persons with migraine (i.e., “let-down” headache). We aimed to test this hypothesis using electronic diaries.

Methods: 20 headache clinic patients with ICHD-2 diagnoses of migraine, age ≥18, who reported 3-10 migraine attacks and < 15 headache days/month were enrolled. Subjects entered data using a palm-pilot device at multiple pre-set and random times daily. The 4-item Perceived Stress Scale (PSS, range 4-20) was assessed daily (PM). Mood was assessed twice daily (rating current feelings of happy, sad, relaxed, nervous, lively and bored from 0-100). Logit-normal random effects models taking account within-person correlation were used to estimate odds of headache.

Results: 17 patients entered ≥30 days of data (996 AM; 1,015 PM entries; 192 headache attacks [mean=5.5]). Lower perceived stress was associated with increased odds ratio (OR) for headache within 12 hours (OR [95% CI] 1.81 [1.13, 2.91] per 4-unit difference on PSS). Improvement (10 point increase) in mood ratings from one to the next day AM to PM was significantly associated with headache occurrence within 12, 18, and 24 hours for happy (ORs 1.20 [1.07,1.36], 1.24 [1.11,1.38], and 1.18 [1.07,1.30] and relaxed ORs 1.26 [1.11, 1.42], 1.17 [1.05, 1.31], and 1.14 [1.03,1.26]. Increases of >10 points were associated with increased ORs for headache within 12 hours (happy OR= 2.73 [1.53, 4.87] and relaxed OR= 2.31 [1.30, 4.11]).

Conclusion: Reduction in perceived stress and increase in feelings of happiness and relaxation were associated with increased odds of headache.

PS2-19

Health resource-utilization (hru) and associated costs by opioid use and dependence among episodic migraine (em): results of the american migraine prevalence and prevention (ampp) study

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Background and aims: To report HRU including healthcare visits and associated costs among persons with EM stratified by opioid use and dependence status.

Methods: EM respondents to the 2009 AMPP survey were divided into 3 groups by opioid use: “never” (no use between 2005-2009), “lapsed” (use between 2005-2008, but not preceding 3 months), and “current” (use in preceding 3 months). Dependence was diagnosed among current users who endorsed ≥3 DSM-IV criteria. Groups were compared using rate ratios (RRs) on visits to healthcare providers, emergency department (ED)/urgent care clinics (UCCs), and imaging. Costs were calculated using Medicare reimbursement rates.

Results: 5,796 respondents were categorized by reported opioid use: never in 5 years: 70.3%, lapsed: 13.8%, and current: 15.9%. 16.6% of current users met criteria for dependence. In comparison to the “never” group, current users had significantly greater odds for healthcare visits to primary-care providers (no dependence, RR=3.37, p<0.001; dependence RR= 8.91, p<0.001); nurse practitioners/physician assistants (no dependence RR=4.21, p<0.001; dependence RR= 11.95, p<0.001); neurologists/ headache specialists (no dependence RR=5.68, p<0.001; dependence RR= 10.36, p<0.001); and ED/UCCs (no dependence RR=4.83, p<0.001; dependence RR= 23.83, p<0.001). Costs were higher for current opioid users compared with the “never” group, and highest within the current use group in those with dependence.

Conclusion: Current opioid users reported significantly greater HRU including more visits to all provider types, ED/UCCs, imaging and higher related monetized costs. Within the current use group, costs were highest among those who met criteria for dependence.

PS2-20

Opioid use, dependence, sociodemographics, medical and psychiatric comorbidities, and headache-related disability among persons with episodic migraine: results of the american migraine prevalence and prevention study

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Methods: Respondents to the 2009 AMPP survey who met ICHD-2 criteria for EM were divided into 3 groups based on reported opioid use:
1. “never” (denied use between 2005-2009),
2. “lapsed” (use between 2005 and 2008, but not in preceding 3 months),
3. “current” (opioid use within 3 months).

Dependence was diagnosed among current users who endorsed ≥3 of 7 DSM-IV criteria. Groups were compared on sociodemographic variables, headache days/month, employment status, medical and psychiatric comorbidities, and headache-related disability (MIDAS). Odds ratios (ORs) and 95% confidence intervals (CIs) were generated characterizing group differences.

Results: 5,796 respondents were categorized by opioid use: never in 5 years: 70.3%, lapsed: 13.8%, and current: 15.9%. 16.6% of current users met criteria for depression. Compared with the “never in past 5 years group”, current users were significantly less likely (ORs < 1) to be married, working full-time, and have annual household incomes of ≥$75,000 (all p < 0.001). They were significantly more likely (ORs >1) to have more headache days/month, greater headache-related disability, meet criteria for depression and anxiety, and report cardiovascular risks/events (all p < 0.001).

Conclusion: Current opioid use was associated with negative outcomes including dependence, worse socioeconomic status, and increased ORs for depression, anxiety, cardiovascular risk factors/events, and greater headache-related disability.

PS2-21
Relationship between high frequency nausea, headache symptomology, and treatment satisfaction in episodic migraine (em): results of the american migraine prevalence and prevention (ampp) study

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Background and aims: Nausea is a defining and debilitating feature of EM. This study assesses headache symptomology and treatment satisfaction/outcomes among persons with EM by headache-related nausea status.

Methods: Respondents to the 2009 AMPP survey who met criteria for EM (ICHD-2 criteria and < 15 headache days/month) provided sociodemographics, headache features, treatment satisfaction, and perceived medication effectiveness (using the Patient Perception of Migraine Questionnaire- Revised [PPMQ-R]). Headache-related nausea was rated as occurring none of the time, rarely, < half the time, or ≥ half the time. Ordinal logistic regression, adjusting for sociodemographics assessed the influence of nausea. Odds ratios and 95% confidence internals were generated.

Results: Among 6,559 persons with EM and nausea symptom data, half (49.7%) reported frequent nausea (≥ half the time) with headache. Frequent nausea compared with none/rare nausea was associated with greater symptom burden for unilateral pain, pulsating pain, pain worsened by activity, photophobia, phonophobia, osmophobia, loss of appetite, neck pain and sinus pain (all p < .001). Respondents with frequent nausea reported more dissatisfaction with medication effectiveness, medication side effects and more dissatisfaction overall (all p < .001) and greater endorsement that headache medication(s) interfered with work, household work, and family social and leisure activities (all p < .001).

Conclusions: Persons who frequently experience nausea with headache also have greater odds of experiencing other headache symptoms, and reporting less satisfaction with current medications, more side effects, and more medication-related interference in several aspects of life. Treating nausea may translate to reduction in the overall burden of migraine for persons with EM.

PS2-22
Frequent nausea in episodic migraine (em) is common and associated with increased burden: results from the american migraine prevalence and prevention (ampp) study

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Background and aims: Opioids carry the potential for dependence among persons with episodic migraine (EM) and may negatively influence other outcomes. We aimed to assess the prevalence of opioid use and dependence and may negatively influence other outcomes.

Methods: Respondents to the 2009 AMPP survey who related disability.
Background and aims: After head pain, nausea is one of the most debilitating symptoms of EM. This study describes sociodemographic characteristics and nausea-related headache burden in persons with EM.

Methods: Respondents to the 2009 AMPP survey who met criteria for EM (ICHD-2 criteria and < 15 headache days/month) provided sociodemographics, headache-related disability (MIDAS), headache pain severity and lifestyle impact (HIT-6) data. Headache-related nausea was rated as occurring none of the time, rarely, < half the time, or ≥ half the time. Chi-square was used to compare sociodemographics. Ordinal logistic regression adjusting for sociodemographics yielded odds ratios (OR) and 95% confidence internals (CI) for MIDAS scale and HIT-6 items.

Results: Among 6,559 cases with EM and nausea symptom data, half (49.7%) reported frequent nausea (≥ half the time) with higher frequency in females (52.6%) compared with males (39.3%, p < .001) and in persons on ‘disability’ or medical leave (62.5%) versus those employed full time (46.7%, p < .001). Individuals with frequent nausea compared with never/rare nausea were twice as likely to experience higher grades of MIDAS disability (OR 1.94, CI 1.68 - 2.24) and four times more HIT-6 “severe pain” (OR 3.71, CI 3.28-4.18) as well as greater headache lifestyle impact (p < .001) on limits to daily activities, desire to lie down, tiredness, irritability and difficulty concentrating items.

Conclusion: Persons with EM who frequently experience nausea with headache fared significantly worse on measures of headache-related disability and headache-impact. Nausea is a debilitating feature of EM and should be considered in selecting treatment.

PS2-23
Pathway ch-1 study: sphenopalatine ganglion stimulation for acute treatment of chronic cluster headache
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Background and aims: The cranial autonomic symptoms and head pain associated with cluster headache result from activation of the trigeminal parasympathetic reflex. The efferent component of this reflex is mediated through the SPG. We aimed to investigate the safety and efficacy of on-demand sphenopalatine ganglion (SPG) stimulation for the acute treatment of chronic cluster headache.

Methods: A multi-center, randomized, controlled, dose range finding study, with a random insertion of placebo, multiple headache, acute treatment study design, has been initiated. All subjects must meet the 2004 International Classification of Headache Disorders (ICHD-II) diagnostic criteria for chronic cluster headache, are dissatisfied with current cluster headache treatments and experience a minimum of 4 cluster headaches per week. Subjects are implanted with a miniaturized neurostimulator using a minimally invasive trans-oral technique, which along with a handheld remote controller provides on-demand electrical stimulation to the SPG. During the study experimental phase, subjects treat each headache using a remote controller which transcutaneously powers the neurostimulator and controls the therapy delivery. Each headache is randomized to one of three therapies (1:1:1) by the remote controller; full stimulation, sub-perception stimulation, and placebo. The primary endpoint, captured by an electronic headache diary within the remote controller, is acute pain relief response by 15 minutes. The primary safety endpoint is the device related serious adverse event rate.

Results: Enrollment in the study has started, and preliminary data from this novel neurostimulation therapy for severe headaches will be available for presentation during the IHS Congress.

PS2-24
Relation between neurophysiological and psychological features in adolescence headache
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Background and aims: Headache involves neurobiological, psychological and environmental factors. In adult patients, abnormalities in Intensity Dependence of Auditory Potentials (IDAP) and habituation have been reported, whereas data in adolescents are scant.
Our study investigates concurrently IDAP and habituation, by means of a newly developed software, in migraine (MwA) and tension type headache (TTH) adolescents and healthy controls (HC), also submitted to psychological assessment.

**Methods:** 40 adolescents (19 M, 21 F; mean age 15.75, DS ± 1.25; according to ICHD-II: 16 MwA, 11 TTH, 13 HC) underwent auditory evoked potentials registration, with 4 intensities randomly delivered in 3 subsequent identical blocks, and psychological assessment (MINI, CBCL 6-18, SAFA).

**Results:** Cases showed a greater IDAP than HC, in Pz derivation (p = 0.013). With regard to habituation, MwA group presented increased habituation regarding more intense tone and less habituation regarding less intense tone (p = 0.025); TTH adolescents showed no significant results. No relation between IDAP had habituation emerged. IDAP and psychological aspects do not show significant relations. Habituation is negatively related to depressive traits (SAFA-D) in TTH group (p < 0.05); no relations emerged regarding CBCL.

**Conclusions:** Results regarding IDAP suggest that MwA and TTH share a common malfunction in input processing. However, also some diagnosis-specific abnormalities in habituation were found. Relations between neuro-physiological and psychological features suggest a potential involvement of some different factors in headache pathogenesis and importance of a multidimensional approach.

**PS2-25**

Sleep bruxism and headache in adolescents: an experimental trial with a mandibular advancement appliance (preliminary data)

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Sleep bruxism (SB) is a sleep-related movement disorder characterized by tooth grinding/clenching and morning jaw muscle pain and headaches. SB is frequently reported in pediatrics. The pathophysiology is partly explained by a re-activation of cerebral and autonomic nervous systems during sleep (sleep arousal), and evidence in literature supports an association between SB and sleep-disordered breathing (e.g. snoring and obstructive sleep apnea). The study aimed at evaluating the efficacy of a mandibular advancement appliance (MAA) for the management of SB and headache in adolescents.

Twelve adolescents (mean age 15.3 ± 0.66) reporting SB and frequent headache (< 1 day/week) underwent 4 ambulatory polysomnographic recordings performed at baseline and when the MAA was worn during sleep. The MAA was used in 3 different positions (A-free splints; B-central occlusion; C-50% advancement) for periods of 1 week each in a randomized order (A-B-C or B-C-A). Headache complaints were evaluated by questionnaires.

Overall, sleep variables were not different between the 4 nights. SB index (episodes/h of sleep) was decreased with the MAA, up to 71% decrease when in the advancement position (p = 0.009; ANOVA). Headache intensity was decrease by 57%, reaching significant values with the MAA in central occlusion (p = 0.04) and advanced (p = 0.05) positions.

These findings suggest that the improvement of upper airway patency obtained with a MAA may be effective in contrasting the occurrence of SB and daytime complaints of headache. However, the interaction between SB, breathing during sleep and headache as well as the long-term efficacy and safety of MAA, need further investigations.

**PS2-26**

Does bruxism and orofacial pain occur more often in headache patients than healthy controls?

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**Background and aims:** Temporomandibular disorders (TMD) and tension-type headache (TTH) are coexisting disorders and both characterized by increased tenderness in the pericranial muscles. The relation between tenderness, sleep quality and oral health in headache patients is unknown.

Our aim was to characterize the TTH patients suffering from orofacial problems.

**Methods:** Consecutive patients from Danish Headache Center who fulfilled the IHCD-2 criteria for frequent episodic or chronic TTH and 50 healthy controls were included.

As a part of a large clinical study patients and healthy controls completed a questionnaire regarding The Research Diagnostic Criteria for Temporomandibular
Disorders (RDC/TMD) and focusing on 5 questions about bruxism and other oral parafunctions.

**Results:** 56 included headache patients (mean age 38 years) and 50 healthy controls (mean age 40 years) completed a baseline questionnaire. Overall, headache patients differed significantly ($p < 0.01$) from healthy controls.

**Conclusions:** Headache patients suffer more frequently from bruxism and orofacial pain than healthy controls. Increased focus is needed.

**PS2-27**

*Study on the prevalence of chronic daily headache with and without medication overuse (the spartacus study)*

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**Background:** Chronic daily headache (CDH) is a disabling condition that includes a heterogeneous group of headaches occurring $\geq 15$ days per month for at least 3 months. To date, there have been no previous general population based studies on CDH in Italy.

**Objectives:** To estimate the 3-months prevalence of CDH with and without medication overuse in a representative sample of adult population.

**Methods:** This was an observational, cross-sectional study. We sent an ad hoc validated questionnaire (sensitivity 97%, specificity 86%) to 25163 adult subjects registered in the lists of 20 GPs in Casalecchio di Reno district. The study population was representative of Emilia-Romagna general population (northern Italy). A self-addressed stamped envelope was enclosed to return the survey.

**Results:** 16409 subjects returned the questionnaire (65.2%), among which 207 (1.26%) were incomplete. 608 (3.7%) subjects resulted affected with CDH (mean age 51.52 $\pm 16.66$ years and mean BMI 25.36 $\pm 4.39$); 228 (1.38% of the whole sample) with medication overuse and 380 (62.5% of CDH) without medication overuse. Prevalence in women was higher than in men in each group (M:F=1:3). 6706 subjects (41%) resulted affected with headache < 15 days per month.

**Conclusions:** CDH with and without drug overuse is a common disorder in the general Italian population, mainly in women. The high rate of answer to our survey was due to GPs direct involvement. Our study highlights the public health impact of this kind of chronic pain that need more attention.

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**PS2-28**

*Headache and menopause: a prospective population based study*

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**Background:** Migraine generally improves after menopause, but prospective studies on headache pre and after menopause are lacking.

**Objective:** The aim was to investigate the effect of menopause on headache.

**Methods:** This is a prospective cohort population-based study conducted in the Republic of San Marino. In 1984 a systematic random sample of 1144 inhabitants was invited to answer a semi-structured questionnaire on headache. Among them, women that were aged between 35 and 50, not yet menopausal, were invited to be interviewed in 2000 if menopausal at this time.

**Results:** We included 72 women. In 1984 mean age was 40.7 (range 33-49): 43 (67.2%) subjects had migraine without aura (MoA), 4 (6.3%) had tension-type headache (TTH), in 3 (4.7%) coexisted MoA and TTH, 2 (3.1%) had migraine with aura (MwA) and MoA, 1 (1.6%) had chronic daily headache (CDH) and 19 didn’t suffered from headache. After menopause, 38 women (52%) changed diagnosis: in 12 subjects (32%) headache disappeared while among women without headache at the first interview, 3 had TTH, 5 had MoA, 1 had CDH, 1 MoA and TTH and 1 MwA and MoA in 2000. A reduction in intensity, frequency and duration of headache was reported after menopause respectively in 31.3%, 40.6% and 29.7% of subjects.

**Conclusions:** We prospectively studied a sample of women in fertile period and after menopause. Headache diagnosis changed in 52% of cases after menopause. Headache, mainly migraine, improved or recovered after menopause but a half of women without headache became headache sufferers after menopause.
**PS2-29**

**Treatment of headaches in the first trimester of pregnancy**

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Experiencing headaches during pregnancy is one of the most common discomforts and complaints. Headaches may occur at any time during pregnancy, but tend to be most common during the first and third trimester. Almost 15% of the pregnancy complaints are migraine attacks. The safety and tolerability of medications used to treat acute migraine attacks are well established. However clinical tolerability profiles and therapeutic benefits treating pregnant women in the first trimester are a serious challenge.

**Background:** Moderate and severe migraine attacks in pregnancy are almost always characterized by attacks of headaches, nausea, vomiting, photo and phonophobia, and they often need hospital treatment.

**Methods:** Ten women, in the first trimester of pregnancy that have been experiencing moderate and severe migraine attacks have been treated. The treatment contained acetaminophen, antiemetic and anesthetics. Triptans and NSAID were excluded due to their adverse affects.

**Results:** The improvement with anesthetic therapy occurred in less than two hours of the hospital treatment. The treatment was then continued with antiemetic and acetaminophen. All ten patients were free of headaches during the next twenty-four hours. The hospital treatment lasted twenty-four to forty-eight hours.

**Conclusions:** Further investigations and treatment options need to be done in this specific group of patients. Choosing proper treatments must demonstrate the balance between efficacy, tolerability and safety.

**PS2-30**

**Estrogen-dependent effect of 5-hydroxytryptophan on susceptibility to cortical spreading depression in rat**

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**Background:** Migraine is considered a “low 5-HT” condition and sexually dimorphic. The 5-HT synthesizing enzyme tryptophan hydroxylase is influenced by estrogens. Reduced 5-HT transmission might cause both deficient pain control and changes in cortical excitability. Cortical spreading depression (CSD), the culprit for migraine aura, is enhanced after 5-HT depletion in rat.

**Objective:** To determine if exogenous administration of 5-hydroxytryptophan (5-HTP), known to increase CNS levels of 5-HT independently of tryptophan hydroxylase, can modify KCl-induced CSD in rat and if the effect differs between males and females.

**Methods:** Adult male and female Sprague-Dawley rats (n=8/group) received intraperitoneal injections of 5-HTP (100 mg/kg) or NaCl 0.9%. One hour after the injections, CSDs were elicited by applying over the occipital cortex a cotton ball soaked with 1M KCl and recorded by DC electrocorticogram. The phases of the estrous cycle were determined by vaginal smears before the electrophysiological recording.

**Results:** 5-HTP administration had no effect on CSD frequency in males. By contrast, in females there was an estrous cycle-dependent effect. In estrus, just after the decrease of estrogen blood levels, 5-HTP decreased significantly CSD frequency, while during proestrus (estrogen peak) it had no effect.

**Conclusion:** These preliminary results suggest that an increase of serotonin levels does not alter the susceptibility to CSD in males while in females the effect depends on gonadal hormone levels. Sex hormone-dependent changes in central 5-HT transmission might thus contribute to the sexual dimorphism of migraine, independently of the known effect of estrogens on tryptophan hydroxylase.

**PS2-31**

**Temporomandibular disorders and cutaneous allodynia are associated with depression symptoms in migraine patients**

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**Background:** The presence of Cutaneous Allodynia (CA) in migraine patients and its involvement in migraine chronification has been reported. However, the association of CA, Temporomandibular Disorders (TMD) and depression could contribute to aggravate such mechanism.
Purposes: To verify symptoms of depression in migraine patients with and without TMD and CA.

Methods: We evaluated 53 migraine patients (18 to 65 years) according to the second edition of the International Classification of Headache Disorders (2004) from a tertiary care outpatient headache clinic. TMD was assessed using Research Diagnostic Criteria for TMD and three subgroups were considered: without TMD (WTMD), Myofascial TMD (MYTMD) and Mixed TMD (MITMD). Symptoms of depression were assessed using Patient Health Questionnaire (PHQ-9). The patients were submitted to the Allodynia Symptom Checklist (ASC-12) and they were divided into four categories: no allodynia (NOCA), mild (MICA), moderate (MOCA) and severe (SECA).

Results: It was verified a significant percentage of mixed TMD patients with depression symptoms in relation to the other groups (MITMD: 36%, WTMD: 15% and MYTMD: 10%, p < 0.0001, chi-square test). It was observed higher score of depression symptoms for SECA group compared to the others (NOCA: 2.45±2.66, MICA: 2.00±1.58, MOCA: 2.75±1.39 and SECA: 4.39±2.95, p < 0.05, ANOVA).

Conclusion: The results suggested that TMD and CA in migraine patients could contribute to the development of depression symptoms and showed the importance of the identification of TMD in migraine patients. Moreover, the association of multiple TMD diagnoses and greater severity of CA could increase the chance to depression symptoms onset.

PS2-32
SUNCT, SUNA and pituitary tumors: clinical characteristics and treatment

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Backgrounds: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) are rare primary headache disorders.

Objectives: To describe a series of patients with SUNCT and SUNA including relationship to pituitary tumors.

Methods: All cases of SUNCT and SUNA in our headache clinic at Foothills Hospital, Calgary, were reviewed.

Results: Six patients (4 SUNCT, 2 SUNA) were found. Age of onset ranged from 20 to 59. Five were female. The pain was severe, unilateral and occurred in orbital, frontal and temporal regions. Sharp, stabbing, knife-like sensations were commonly described. Attack duration ranged from 3-120 seconds and attack frequency was 1-100 per day. Autonomic symptoms were present in all cases. MRI showed pituitary adenomas in 5 out of 6 patients. The pituitary tumor was on the same side as the pain in all patients. Four of 5 underwent surgery. Pathology included three prolactinomas, and one mixed adenoma and gangliocytoma. One patient with complete removal has remained headache free for 4 years. One patient was pain free for a year, but headaches returned with tumor recurrence. Another patient had major improvement, and one has not improved after surgery. Patients were generally refractory to medications, although one without a tumor had a good response to verapamil.

Conclusions: Our patients showed typical symptoms of SUNCT and SUNA. Five of six patients had pituitary adenomas. Tumor removal resulted in major improvement in three of four patients. Medical treatment was only partially effective.

PS2-33
Disability by migraine and probable migraine in Korea: result from Korean headache survey

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Background: Migraine and probable migraine are common headache disorders which are often severely painful and disabling. Disability of migraine and probable migraine were not assessed yet in Korea. We conducted this study to assess disability by migraine and probable migraine in Korea.

Methods: Korean Headache Survey is a nation-wide cross-sectional descriptive survey that was conducted using a structured interview using questionnaire to determine the status of headache disorders of adults aged 19 or older by interviewers, conducted in March 2009. For assessing disability, respondents were asked to identify missed or reduced productivity for work, school or
household because of your headaches in last 3 months. If respondents had missed or reduced productivity by headache, they were asked days for miss or reduced productivity days.

**Results:** Among Koreans of 19 years old or above, we randomly selected 1,507 by stratified random sampling. Prevalence for migraine was 6.0% and prevalence for probable migraine was 11.5%. 11.1% of migraine suffers and 17.1% of probable migraine suffers reported that they missed work, school or household in last 3 months. Mean missed days for migraine was 3.00±1.73 days and for probable migraine was 3.81±7.80 days during last 3 months. 28.1% of migraine suffers and 17.0% of probable migraine suffers reported that they suffered reduced productivity in work, school or household in last 3 months. Mean reduced productivity days for migraine was 2.96±3.00 days and for probable migraine was 4.69±9.79 during last 3 months.

**Conclusions:** Migraine and probable migraine imposed significant amount of disability in Korea.

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**PS2-35**

Factors associated with severe impact of migraine: result from Korean headache survey


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**Background:** Migraine is a heterogeneous condition that results in a spectrum of impacts on individuals. Understanding factors associated with severe impact of migraine is an important step towards optimizing interventions. We conducted this study to describe factors associated with severe impact of migraine.

**Methods:** The Headache Impact Test-6 (HIT-6) is a six-item questionnaire to assess the impact of headache including migraine. HIT-6 assesses the impact of headache as little or no impact (0-49), some impact (50-55), substantial impact (56-59) and severe impact (60+). We selected a stratified random sample of Koreans over age 19 and evaluated them with a 12-item semi-structured interview designed to identify headache type using ICHD-2. Factors associated with severe impact were assessed in univariate and multivariate analyses.

**Results:** Of 1,506 participants, 91 were diagnosed as having migraine (6.0%). 39 (42.0%) had little or minimal impact, 23 (25.7%) had some impact, 12 (13.0%) had substantial impact and 17 (18.5%) had severe impact. In univariate analyses, aggravation by routine physical activity (OR=2.722, 95% CI=1.019-65.475, p=0.048),
photophobia (OR = 6.054, 95% CI = 1.658-22.107, p = 0.006), phonophobia (OR = 11.714, 95% CI = 1.715-79.999, p = 0.012) and visual aura (OR = 1.936, 95% CI = 1.042-3.600, p = 0.037) were associated with severe impact. Taking less than 4 headache days per month as the reference, ≥15 headache days per month was associated with severe impact (OR = 13.172 95% CI = 3.808-45.557), p = 0.025). In the adjusted multivariate analyses, association of factors with severe impact disappeared.

Conclusions: These results demonstrated that a significant proportion of migraineurs had severe impact and there are some factors associated with severe impact of migraine.

PS2-36
Exploring the structure of migraine diagnosis across the population sample: factor analysis of ichd-ii migraine diagnostic criteria


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Background & aims: In the absence of etiologic gold standard of migraine, the ICHD-2 diagnostic criteria for migraine is composed of headache features, associated symptoms, attack number and attack duration. Factor analysis is a statistical method used to describe variability among observed variables in terms of a potentially lower number of unobserved variables. For better understanding of the structure of ICDH-2 migraine diagnosis, we conducted factor analysis of migraine diagnostic criteria using Korean Headache Survey data.

Methods: Korean Headache Survey is a stratified random population sample study of Koreans over age 18 and evaluated them with a 12-item semi-structured interview designed to identify headache type using ICHD-2, conducted in March 2009. An explanatory factor analysis (EFA) and a series of confirmatory factor analysis (CFA) were conducted on 9 variables after ICHD-2 criteria using data of migraine suffers.

Results: Of 1,506 participants, 91 were diagnosed as having migraine (6.0%). In the EFA, two- and three-factor models emerged. Two-factor model corresponded phonophobia, aggravation by routine physical activity, photophobia and osmophobia/ moderate-to-severe pain and vomiting. Three-factor model corresponded phonophobia, aggravation by routine physical activity, photophobia and osmophobia/ unilaterality and nausea/ vomiting and moderate -to-severe pain. The results of the CFA suggested that a two-factor model improved the fit.

Conclusions: The ICHD-2 diagnostic criteria for migraine could be parsed into 2 partially related factors across population sample. Further efforts to elucidate the structure of migraine diagnosis may be facilitated for understanding the nature of the disease.

PS2-37
Prevalence and impact of chronic daily headache in korea: result from korean headache survey


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Background and aims: Chronic daily headache (CDH) is an umbrella term for headache disorders that occur very frequently. CDH is usually associated with medication overuse and imposed a significant amount of impact on individuals. Prevalence and impact of CDH were not assessed in Korea yet. We investigated prevalence and impact of CHD in Korea using Korean Headache Survey data.

Methods: We selected a stratified random population sample of Koreans over age 19 and evaluated them with a 12-item semi-structured interview designed to identify headache type using ICHD-2. We defined chronic daily headache including ≥15 headache days more than 3 months at the time of interview. Medication overuse is defined as medication use for headache ≥3 days per week more than 3 months. We also assessed the impacts of CDH on individuals using HIT-6 questionnaire.

Results: Of 1,506 participants, Twenty seven (1.8%) of them had CDH (1.5% in men and 2.2% in women).
Seven of them (27.9%) were associated with medication overuse. Prevalence of CDH was highest in aged 60+ (1.7% for 19-29, 1.1% for 30-39, 1.2% for 40-49, 2.0% for 50-59, 4.3% for 60+). 39 (21.6%) had little or minimal impact, 23 (28.3%) had some impact, 12 (19.4%) had substantial impact and 17 (30.7%) had severe impact.

**Conclusions:** Prevalence of CHD was 1.8% and medication overuse was associated in 27.9% of them. CDH imposed a significant amount of impact on CDH suffers in Korea.

**PS2-38**

Management of headache in concussed athletes

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**Objective:** To define, describe and discuss current treatments for professional, elite and amateur athletes who suffer from acute and chronic post traumatic headache as a result of sports related concussion.

**Methods:** A Pub Med search was conducted using the key words; “acute and chronic post traumatic headache in sports”, “sports concussion and headache”, “post traumatic migraine and sports”, “acute and chronic post traumatic headache and sports related concussion”, “management of headache in sports”. The results returned a total of 84 articles which were either case reports or opinion papers. No evidenced based studies were found.

**Results:** Headache is the most common symptom of sports related concussion occurring in up to 88% of all sports related concussions. Approximately 15% of all athletes who suffer a sports related concussion will go on to develop chronic post traumatic headache. Athletes have unique physiological and social issues which need to be considered when developing a treatment protocol for acute and post traumatic headache management.

**Conclusion:** Evidence based studies are required to determine what therapies are appropriate for athletes of all levels who suffer acute and chronic post traumatic headache as a result of sports related concussion. Further research is also needed on the mechanism of sports related post traumatic headache as it relates to the pathophysiology of sports concussion.

**PS2-39**

Trigeminal autonomic cephalalgias in the first neurological assessment

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**Background and aims:** To study the clinical profiles, imaging findings and outcomes in 31 patients in their first neurological assessment for a Trigeminal Autonomic Cephalalgia (TAC) and TAC-like syndromes.

**Methods:** We followed prospectively 31 patients recruited in the Outpatient clinic of the Neurology Department during 2010 (18 male, mean age at onset 40.2 +/- 5 years) presenting with TAC or TAC-like syndrome in their first neurological assessment. All patients had a clinical picture fully compatible with a TAC, including 6 patients in which a structural lesion could be found. There was a significant improvement or even disappearance of the headache after therapeutic in symptomatic cases.

**Results:** 26 patients (83.8%) were referred to the Neurology Outpatient Clinic by their family Physicians and from those, only 12 (46.1%) had a previous correct management and diagnostic approach. Primary cases included 21 Cluster Headaches (64.5%), 2 short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) and 2 with paroxysmal hemi-crania. Six patients had secondary causes (19.3%), including two carotid dissections, one ethmoid sinusitis, one maxilar sinusitis, a pituitary adenoma and one had a meningioma in the cavernous sinus.

**Conclusion:** Our study found that CH was the most common cause of TAC. We found that even typical TACs can be caused by an underlying lesion. Clinical warning signs and symptoms could be rare. Neurological assessment and neuroimaging in patients with a TAC or TAC-like was crucial for diagnosis.

**PS2-40**

Analysis of patients attending a new specialist irish headache clinic


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This study analysed the profile of 200 patients who were new referrals to an Irish specialist headache clinic.
A retrospective audit was conducted of 200 new patients referred to a newly established specialist headache clinic at the Mater Misericordiae Hospital in Dublin between January 2010 and January 2011.

70% of patients were referred to the Headache clinic by GPs with the remaining 30% being referred by other medical specialties. 58% of the patients referred were female. 60% were under the age of forty while only 5% of new referrals were over sixty. A consultant neurologist with a specialist interest in headache saw 98% of the patients, either alone or with a neurology registrar or headache specialist nurse. 93% of patients were diagnosed with migraine (70% chronic, 30% episodic). The remainder of patients were diagnosed with cluster headache, paroxysmal hemicrania, temporal arteritis, trigeminal neuralgia, TACS and headache with a possible secondary cause. MOH was present in 52% of our cohort with the majority overusing paracetamol and codeine based medications. Almost 71% of patients attending the clinic with migraine had never been on prophylactic therapy. 148 patients attending our clinic were started on prophylactic agents-the most commonly prescribed one was amitryptiline, followed by topiramate and flunarazine.

Migraine was significantly the most common headache type encountered in this Irish secondary-care clinic. Review of treatment patterns used prior to the initial clinic evaluation suggests that management of migraine in Irish primary care is suboptimal, and educational initiatives are needed to improve headache management.

**Results:** We received an answer from 16 subjects (5 male, 11 female; average age of 35.8 years old). The average time from the beginning of 3-D videos to headache expression was 69 minutes, and the average duration of headache was 7 hours 49 minutes. Only 2 cases experienced headaches caused by ordinary 2-D videos. The location of the headache was bilateral in 12 cases and a non-pulsating quality was noted in 13 cases. The intensities of the headaches were as follows; mild in 6 cases, moderate in 6 cases, and severe in 4 cases. Nine of 16 cases did not usually have headaches. Three of 7 cases who usually had headache responded that the headaches caused by 3-D videos were different from ordinary headaches.

**Conclusions:** The 3-D headache might therefore be a new type of headache because most of the cases were not provoked by ordinary 2-D videos, and the qualities of the 3-D headache are also different from 2-D headaches.

**PS2-42**

Patho-physiological assessment of hormonal state of hypophys-ovarian and hypophysis - adrenal axes and an anxiety-depression component in formation of tension-type headaches in patient

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Tension-type headache is the most spread among primary cephalgies. Women suffer from tension-type headaches three times often than men.

Psycho-emotional status and concentrations of hypophys-ovarian and hypophysis - adrenal hormones were studied in 230 patients of reproductive age who had tension-type headache.

Of them, 150 women with chronic and 80 with episodic tension headache were examined.

It was found that in case of chronic tension headache, the increased hormones, i.e. in follicle phase: FSH (follicle-stimulating hormone) (18,2±1,4 IU/L) and LH (luteinizing hormone) (52,2±7,5 IU/L); in luteinizing phase: progesterone (89,7±3,6 nmole/L); in both phases: estradiol (274,3±25,3 pg/ml), testosterone (2,4±0,3ng/mL) and cortisol (877,2±35,6 nmole/L) were accompanied by moderate anxiety and evident depression.
The women with episodic tension headache demonstrated low anxiety and their hormones in serum were within the normal range.

The obtained data allow us to trace the pathogenic correlation among chronic tension headache and hormonal deviations.

PS2-43
Olfactory hallucination in primary childhood headaches
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Background: Reports of olfactory hallucination (OH) in the paediatric population are particularly rare1,2.

Aim: His study examines the incidence of OH and its characteristics in primary childhood headaches.

Methods: 863 patients were eligible for the study, 503 affected by migraine, 140 by tension-type headache, 78 by other headaches and 142 by headache not elsewhere classified. Headache diagnosis was based on the ICHD-II criteria. OH was examined among patients using a semi-structured questionnaire or headache diary. In this study, OH refers to perceived smell in the absence of odorant stimulation.

Results: OH was found among ten patients (ages ranging from 6.9-15.5 years) during headache attacks. OH included smells such as rotten cheese, burned plastic, fish tanks, corned beef or burned sweat. They developed and disappeared gradually and lasted between 15 and 40 minutes. OH was not present in between headache attacks and the smells were not experienced by others at the time. Headaches among these patients were never triggered by smell of any kind. Use of pain killers did not help with OH. Headache diagnosis amongst these patients included MA (n=7) and MO (n=3).

Conclusion: This study demonstrates that OH does occur in childhood migraine. We will discuss how our findings could provide scientific evidence for the application of ICHD in childhood headaches.

References:

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PS2-44
The effectiveness of trigger point injection for the treatment of acute exacerbation of cervicogenic headache
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Background and aim: Treatment of cervicogenic headache is considered a challenge as its anatomic, pathophysiologic symptoms and complexities can be similar to migraine. Our objective is to evaluate the effectiveness of trigger point injection (TPI) applied to cervicogenic region in the management of acute exacerbation of cervicogenic headache.

Methods: 103 patients were evaluated according to IHS classification of secondary headaches. Patients were allocated to receive either TPI (N-51), or IV infusion (N-52), as per patients’ preference. TPI containing 40mg Methylprednisolone diluted in 4ml of Bupivacaine 0.25% were bilaterally injected to the cervicogenic region including sub-occipital, upper-trapezius and mid-trapezius. The IV infusion containing: Ketroxolac 30mg; Promethazine 25mg and Diphenhydramine 50mg was administered intravenously over 30 minutes. Trial was conducted over a 2-year period at the Pain & Headache Center, IMC, Jeddah, K.S.A. Inclusive criteria: 51 males, 52 females; ages between 20-50 years, with a mean of 35. Exclusive criteria: pediatric patients; patients older than 50, with uncontrolled diabetes, blood pressure, and other neurological deficits.

Results: Average improvement of 80 %, according to numeric pain scale, was seen in patients within 10 minutes of TPI and lasted for an average of 72hrs as patients continued to improve with initiation of preventive therapy. However, an average improvement of only 60% was appreciated within 30 minutes of IV infusion and lasted for only 24hrs as patients continued to improve as per above.

Conclusion: Patients who received TPI showed more rapid, significant, and sustained improvement compared to patients who received the IV infusion.

PS2-45
The effectiveness of etoricoxib in the treatment of severe exacerbation of chronic daily tension headache (cdth)
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Program Abstracts
Background and aim: Most common among adults, “tension-type” headaches may appear periodically (episodic, less than 15 days/month) or daily (chronic, more than 15 days/month), these headaches may last from 30 minutes to several days. Chronic daily tension headaches (CDTH) come and go over prolonged period. Our objective is to evaluate the effectiveness of Etoricoxib tapering in the treatment of severe exacerbation of CDTH.

Method: 200 patients, evaluated according to IHS classification at the Pain & Headache Center, IMC, KSA, were randomly allocated to receive either Etoricoxib tapering alone or in combination with Cyclobenzaprine for 6 months. First group (N=106) received Etoricoxib tapered over 30-day period (60mg BID [10days], 90mg OD [10days], 60mg OD [10days]) in combination with Cyclobenzaprine 5mg daily at bed time for 6 months. Second group (N= 94) received only Cyclobenzaprine 5mg at bed time for 6 months. Inclusive criteria: 80 males, 120 females; ages between 25-60 years, with a mean of 43. Exclusive criteria: pediatrics, patients older than 60, with uncontrolled diabetes and blood pressure; pregnancy and other neurological deficits.

Results: Average improvement of 80%, as per numeric pain scale, was seen in patients receiving combination therapy (Etoricoxib and Cyclobenzaprine), appreciated within 3 weeks and sustained for 12 months. However, an average improvement of only 55% was seen in patient receiving Cyclobenazpirne alone, appreciated within 6 weeks and sustained for only 9 months.

Conclusion: Patients receiving Etoricoxib and Cyclobenzaprine showed more significant, faster symptomatic improvement and sustained effect for longer period than those receiving only Cyclobenzaprine.

PS2-46
Comparing the quality of life in three primary headache types with frequent attacks

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Background: Previous comparative quality of life (QOL) studies focused mostly on the episodic form of migraine, despite the fact that the number of attacks and headache days are smaller in episodic migraine than in chronic tension type headache and in the active phase of cluster headache.

Aim: To study the effect of chronic migraine (CM), chronic tension-type headache (CTTH) and cluster headache (CH) on generic and headache-specific QOL.

Method: Consecutive outpatients completed the SF-36 generic and the CHIQ headache-specific QOL questionnaires. Kruskall-Wallis ANOVA with post-hoc Dunn tests was used for the statistical evaluation of the QOL scores.

Results: 74 patients (48 females; mean age 39.9 ± 14.4 years; diagnosed with CM /N=22/, CTTH /N=32/ and CH /N=20/) were studied. Four of the 8 SF-36 domains showed significant differences across the diagnostic groups: The bodily pain domain was most severely affected in CH; physical functioning, general health perceptions and vitality were lowest in the CM group. The CHIQ's physical, mental and social dimensions and total score showed significant differences between headache diagnoses. Headache-specific QOL was numerically most reduced in CH, but the post-hoc tests showed that the differences between CH and CM patients were statistically not significant in this population.

Conclusion: Different types of frequent primary headaches affect generic and headache-specific QOL in different patterns. Chronic migraine seems to affect generic QOL more than the other two headache types. The effect of chronic migraine and cluster headache is probably more severe on headache-specific QOL than that of chronic tension type headache.

PS2-47
The comparison of the group of cognitive-behavioral therapy effect on depression and disability feeling results from headache in patients having tensional headaches

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Background and objective: International society has defined headache and tensional headache in adults as headache attacks occurs at least 15 times a month and lasts for over 6 months.

Different authorities have found depression as the most incident psychological disorder in patients having headache.

Also the privilege of depression has been considered in different types of headache.
The purpose of this study is to consider and compare the effect of cognitive-behavioral therapy method on undesirable issues of headaches from disability of headache and depression in life and educational function of patients having headache.

**Method:** Among the female university students of the dormitory of Gachsaran Islamic Azad University, subjects assigned for experimental and control groups simply randomly and according to diagnostic interviews, neurologist diagnosis, medical documents. During 16 weeks, they participated each week in one 90min therapy session (one educational term).

In this study from the questionnaire of the assessment of disability resulting from headache and depression questioner were used.

Also their study average scores before and after therapies were compared.

**Findings:** Cognitive-behavioral group therapy method caused decreasing of pain of headache and depression patients having headache significantly (p < 0.001).

**Conclusion:** Cognitive-behavioral therapy method can be used as an independent method or beside other therapeutic methods in therapy of lateral variables of tensional headaches, depression and disabilities from headache.

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**PS2-48**

**Atypical melkersson-rosenthal syndrome: a case report**

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**Introduction:** Melkersson-Rosenthal Syndrome (MRS) is an idiopathic, rare disorder characterized in its classical form by a triad of recurrent facial nerve paralysis, swelling of the lips and lingua plicata. However, this classical triad is rarely present, while the monosymptomatic or oligosymptomatic forms are more frequent. As described in literature it can be related to sieronegative oligoarthritis and to lymphoscintigraphic documented impairment in lymphatic drainage from the swollen area.

**Case presentation:** A 40-year-old Caucasian woman, with past medical history of psoriatic arthritis, _H pylori-related gastritis and Spasmophilus_, presented to our department with an history of monthly episodes of weakness, numbness and tingling-burning dysesthesia in the face right accompanied to hypogeusia, dysphonia and dysphagia. These symptoms were always preceded by occipital tension-type headache with transient clouding of vision and edematous appearance of the face right and were responding to prednisone (up to 50 mg per day). MRI with Gd of brain and right cerebellopontine angle, serum tumoral markers’ research, VEP, EMG, ENG and liguoral findings were all normal. A lymphoscintigraphy of right laterocervical and mandibular angle lymphonodes documented an impaired lymphatic drainage, without restoration of lymphatic flow. At three months follow-up episodes were unchanged in frequency: despite of this, headache was significantly responding to treatment with amitriptyline.

**Conclusions:** Differently of what described in past literature we haven’t documented any restoration of lymphatic flow during lymphoscintigraphy nor clinical improvement in this case because of persisting of swelling face, headache and cranial polyneuritis.

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**PS2-49**

**Novel approach to treating chronic tension type headache with botulinum toxin type a**

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**Background and aims:** Over the last decade, the role of Botulinum Toxin in headache prevention has been explored both experimentally and clinically. The results of various trials have shown mixed evidence of efficacy. We propose a novel approach to the treatment of chronic tension type headache by altering abnormal biomechanics in the neck and shoulder region utilizing a focused active rehab program along with Botulinum Toxin Type A.

**Methods:** Five patients with chronic tension type headache and forward head posture were treated with Botulinum Toxin Type A (Botox®) into primary target muscles (upper trapezii, levator scapulae, pectoralis minor and splenius capitis and semispinalis capitis). Patients were required to participate in a focused scapular stabilization rehab program.

**Results:** There was an overall decrease in mean number of headache days from pre-treatment (25.4 days) to post-treatment (8.2 days). The mean number of headache episodes decreased from 44.6 to 7.2 over the course of the study period. Headache severity (VAS scale) was reduced from 6.8/10 to 2.2/10. The SF-36 Health survey scores improved in all patients. Postural deviation was also improved with combination of Botulinum Toxin Type A and an active rehab program.
Conclusion: The combination of Botulinum Toxin Type A injections with a focused active rehab program improves postural abnormalities in the Cervico-thoracic region, and consequently, improves chronic tension type headaches.

PS2-50

A cross sectional study on headache frequency and characteristics in cocaine users

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Background: The association between cocaine and headache has been investigated so far using retrospective studies, surveys with self reported questionnaires or case reports.

Aims: To detail the frequency and characteristics of headache in a consecutive series of cocaine users using the last IHS classification criteria with face to face interviews.

Methods: Cross sectional study on consecutive subjects with cocaine use attending a Drug Addiction Service from 1/8/10 to 31/12/11. Subjects were visited by a psychiatrist (VO) who gathered detailed information on cocaine use, concomitant psychiatric disorders or therapies and other comorbidities. They were then interviewed by a neurologist (LF) on the presence of lifetime and/or current headache, focusing on headache characteristics and on the correlation between headache onset and cocaine use.

Results: We enrolled 80 subjects. Seventy-two (90%) had lifetime or current headache. Twenty-nine suffered from a pre-existing headache (MwA=17, probable MwA=6, TTH=4, other=2). Forty-three started suffering from de novo headache following cocaine use (cocaine-induced headache=2, MwA=18, probable MwA=8, TTH=9, other=6). We found no demographic or clinical differences between subjects without headache, patients with pre-existing headache and those who developed headache only following cocaine use.

Conclusions: Cocaine users very frequently develop de novo headache following drug use. Interestingly, in these subjects, migraine or migraine-like headache are the most common headache (60.5%) while cocaine-induced headache seems to be rare (4.7%).

PS2-51

Improvement of the system of doctors’ training for management of patients with headaches

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Objective: Being a major health problem in Russian Federation, headache is also associated with a certain financial burden (which is equal to 88.4 billion roubles per a year for migraine alone). In order to solve the problem, urgent measures should be taken, including improvement of doctors’ professional skills. The purposes of the research are to evaluate and improve the system of doctor’s training for management of patients with headaches in Russian Federation.

Methods: Sociological survey, questionnaire survey, expert estimation and direct observation were used to evaluate strategies of management of headache patients in three outpatient’s clinics of Moscow and the system of doctors’ training in several educational institutions.

Results: 21% of 298 patients reported on poor professional skills of doctors, who used to mistake in diagnostics (14%), treatment (15%) and prophylaxis (20%).Assessment of curricula for training of general practitioners and neurologists (involved in management of headaches) has demonstrated that they do not meet standards of European Headache Federation. It seems reasonable to elaborate new curricula for advanced training courses at postgraduate level. The course program should schedule both theory and practical training: 8 hours of lectures and 26 hours of practical training for general practitioners, and 24 and 72 hours for neurologists, respectively. 9 new multi-field specialized centers should be also founded in Russia for further improvement of medical aid quality and doctors training.

Conclusion: Improvement in doctors’ training helps to increase effectiveness of medical aid in headaches by 15-20% due to better diagnostics, treatment and prophylaxis.

PS2-52

Cognitive functions in school children and adolescents with primary headaches-neurophysiological and psychological studies

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Introduction: Primary headaches particularly migraine can be one of the important factors disturbing cognitive functioning of school children and adolescents especially the accomplishment of tasks connected with education.

The aim of the study was to estimate some chosen aspects of cognitive and intellectual functioning of children and adolescents with primary headaches: migraine and tension type headaches (TTH).

Material and methods: 90 patients with migraine and 35 with TTH aged 8-18 years were diagnosed according to the revised criteria (IHS 2004). Control group consisted of 66 healthy peers of the same age. Visual and auditory event related potentials particularly P300 were recorded according to IFCN standards. A battery of selected psychological test were used which involved broad domains of intelligence; general intellectual functions, memory, cognitive capacity and perception.

Results: Significant differences in cognitive functions were stated between the examined groups. Patients with migraine beside to children with TTH show important disturbances in ability of short-term visual memory and visuomotor integration. Prolongation of the latencies of event related potentials as well as the rise of their amplitudes were estimated using both forms of stimulation in patients with migraine in comparison to TTH and control group.

Conclusion: Neurophysiological and psychological results confirm the presence of disorders of attention and the process of learning and of memory in school children and adolescents suffering from migraine.

PS2-53
Arterial hypertension in patients with tinnitus
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Background and aims: Due to the high number of heterogeneous etiologic factors in subjective and objective tinnitus a complex approach in differential diagnosis is crucial. Although arterial hypertension belongs to the most important factors of origin and lasting of tinnitus, our experiences point out, that her diagnosis is devoted an insufficient attention.

Methods: We have examined with ambulatory blood pressure monitoring (ABPM) a group of 36 individuals (16 women, 20 men) with the mean age of 46 years (range from 34-64 years) and tinnitus duration from 4 months to 6 years. 24-hour ABPM device Cardiosoft-Tonoport was used and during hearing examination we defined frequency and the level of tinnitus by Clinical Audiometer AC 40, Interacustics.

None of the group member has previous known diagnosis of arterial hypertension or use of any medication altering blood pressure level.

Results: The average values of blood pressure during ABPM were 140/89 mmHg. In day-time phase and night-time phase the average values were 143/91 mmHg and 130/81 mmHg, respectively. 12 persons (33 %) had normotension, but 24 persons (66 %) had hypertension with the average blood pressure values more than 130/80 mmHg.

Conclusions: Our results showed that in a group of patients suffering from tinnitus, arterial hypertension has very high prevalence (66 %). Although diagnosing an treatment of arterial hypertension could not necessarily lead to cessation of intensity of tinnitus, treatment and normalization of blood pressure can decrease the risk of complications of hypertension e.g. myocardial infarction, stroke, heart or renal failure.

PS2-54
Evaluating the performance of id-migraine, ms-q and midas scales in portuguese clinicians
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Objective: To evaluate the performance of ID-Migraine, MS-Q (Migraine Screen Questionnaire) and the MIDAS (Migraine Disability Assessment) scale on Portuguese clinicians, evaluating general practitioners and neurologists analyzing their own headaches.

Methods: Prospective observational survey of general practitioners and neurologists in Portugal in a 5 month period. Data collection was accomplished using anonymous questionnaires with demographic data, headache and migraine status and the ID-Migraine, the MS-Q and the MIDAS score.

Results: Of 348 respondent physicians, 24.4% were neurologists, 53.8% were females and age average was 47.7
Sixty-two physicians (34.3%) were self-diagnosed as migraine, with accuracy for ICDH-II probable of definite migraine of 96.7%. This sample had an average MIDAS score of 8.85 ± 11.3. ID-Migraine presented a sensitivity of 0.89 (95% CI 0.78-0.94), specificity of 0.84 (95% CI 0.75-0.90) and positive predictive value of 0.79 (95% CI 0.68-0.87) for the diagnosis of Migraine while MS-Q had a sensitivity of 0.68 (95% CI 0.55-0.78), specificity of 0.95 (95% CI 0.88-0.98) and positive predictive value of 0.89 (95% CI 0.77-0.95).

Conclusion: Portuguese physicians are able to diagnose Migraine accurately. MIDAS scores revealed mild disability of Migraine in this population. The Portuguese version of ID-Migraine had a good performance in migraine diagnosis, being more sensitive yet less specific than MS-Q. Very few diagnostic and evaluation tools are available in Portuguese and validated for our population, yet the need for validating new scales should be balanced with their utility.

Financial support: This study was supported by Almirall in collaboration with the Portuguese Headache Society.

PS2-55

Headbook.me: a new social network for headache sufferers against migraine and headache

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Aims: Easy sharing of knowledge and information and benefiting from other people's experience is possible with social online networks. For example, Facebook is an internationally used platform to stay in touch with friends across the globe and to stay updated about what they are doing. Further developments are social communities, which concentrate on specific areas of interest. For migraine and headache sufferers, the social network Headbook was created.

Methods: People interested in migraine and headache treatment can present themselves at www.headbook.me with their own profile page, create individual blogs, discuss topics in specific sub-groups, share documents, photos, videos, information and experience. The network is available in German at present. It is actively moderated by users and experts of a headache centre.

Results: The platform is used by around 7000 visitors daily from the German-speaking countries. Users have created 52 topic areas. 64% of visitors return on a regular basis and use the social network 22 minutes per day on average. 97% rate the available information for the practical treatment of their headache as highly relevant.

Conclusion: Headbook is a modern way of permanent information exchange and increasing knowledge about all areas of migraine and headache. It is intensively used as an active self-help group, available 24 hours a day. Up-to-date Expert knowledge is made available to the network on a regular basis to aid practical and efficient healthcare.

PS2-56

Migraine-app: education for clinicians and headache sufferers, monitoring of progression and success of migraine- and headache therapy using an application for the apple's iphone

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Aims: Modern information technology and new mobile phone devices (smartphones) allow the portable usage of the internet. Exchange of information and data are constantly possible. The aim was the development of an application ("App") for Apple's iPhone providing information about current possibilities for diagnosis and therapy of headache disorders. The headache progression can be documented, stored and evaluated by both the patient and the treating doctor.

Methods: The App provides information, basic guidelines and a glossary for migraine and headache therapy. A pain calendar documents the headache phenotype, the treatment and the efficacy. Treatment statistics are evaluated. Warnings are displayed if the risk for medication overuse headache is high. Headache experts of the national headache treatment network can be localised. The diagnostic criteria of the IHS-classification can be accessed. The practicability of the app in everyday use was examined throughout the development phase.

Results: 96% of users judge the practicability of the App as very good. 94% rate the provided basic guidelines for migraine- and headache therapy as very important for an effective treatment. 98% rate the use of the on-line migraine and headache calendar as very useful for the continuous evaluation of therapy success.

Conclusion: Through mobile use of the internet, patients and doctors can continuously document and exchange information and analyse data. The treatment of migraine and headache disorders becomes more transparent and effective for all participants.
PS2-57

Long-term and sustainable reduction of work incapacity as a parameter for risk-sharing in integrated care of headache disorders

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Aims: Based on long-term analyses of therapeutic efficiency of coordinated care in the treatment of headache disorders, we realized a risk-sharing model for integrated headache care the first time. The aim was to find out whether coordinated care of headache disorders results in long-term employability of patients who were previously unable to work.

Methods: Risk-sharing is carried out using a merit-rating system, with which health insurance providers directly and objectively measure capacity to work of the patients. Due to German legal requirements, doctors must report days of absence from work to the insurance providers, which monitor and log days of absence from work, because they need to compensate the employer for these. The insurance providers therefore carry the risk of direct and indirect treatment results on their own. The added costs of a high-intensity treatment concept are only off-set if the treatment outcomes result in a significant reduction of indirect costs (e.g. reduction of work incapacity). Accordingly, insurance providers reward the healthcare provider with a bonus payment if long-lasting capacity for work can be demonstrated. In the case of lack of efficacy, a malus payment must be returned to the insurance company.

Results: The long-term evaluation shows that risk-sharing is a win-win-situation for all participants: in 84.7% of cases, a bonus was paid, a malus only in 15.3%.

Conclusion: Coordinated and integrated care for the treatment of headache disorders and risk-sharing models represent a win-win situation for all participants.

PS2-58

Long-term analysis of quality of life, costs, work- and social situation after treatment in a tertiary headache centre as part of an integrated care network

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Aims: Treatment of headache disorders has to be permanently developed and optimised through continued evaluation of treatment outcomes. Medical treatment innovations have to be continuously integrated. This should result in maximisation of treatment quality. The medical and economic efficacy of specialized and coordinated care in the treatment of headache disorders at the Kiel Headache Centre was externally and independently evaluated across five years by German statutory health insurers.

Methods: Costs, income, work- and social situation and quality of life of individual headache patients were analysed and evaluated by the statutory health insurer continuously across five years. Patients with identical diagnosis, age and sex but without coordinated care were used as controls.

Results: Compared to the control group, patients receiving coordinated care had significantly better outcomes, including longer-term pain reduction, improved employability, improved income situation as well as a reduction in treatment costs.

Conclusion: Long-term analysis shows, that coordinated care is both more effective and cheaper than traditional, non-coordinated care. Headache patients benefit from a higher quality of life. Employers and society benefit as well due to cost savings.

PS2-59

Development and organisation of a nation-wide headache treatment network in germany

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Aims: The traditional treatment of headache patients involves care in separate sectors of the healthcare system. Many sufferers with chronic headache, frustrated with this lack of efficiency, look for alternative treatments outside of the professional system. In the long-term, headache disorders are thereby maintained and aggravated. Severe organ complications then bring patients back to medical care. This results in a marked individual burden as well as very high direct and indirect costs to society.

Methods: Contrasting with the traditional model, a nationwide treatment network of medical specialists in both outpatient centres and hospitals was developed in Germany for the specialized treatment and coordinated care of headache disorders. The participating therapists treat according to current scientific guidelines. Outpatient, rehabilitation and inpatient therapy are harmonised and tightly coordinated. Patients are actively
involved through information, education and self-help group.

Results: Across Germany, more than 452 regional pain therapists in outpatient centres and hospitals collaborate as part of a national treatment network. Local doctors can be found on the network's website. The network is used widely and increasingly. At present, almost all large German statutory health insurers participate in this treatment project. The cost effectiveness has been confirmed through analysis of direct and indirect costs.

Conclusion: The development of this coordinated headache treatment network in Germany has progressed very successfully and is heavily utilized. With its introduction, the national landscape for specialized headache treatment has changed markedly. This confirms the innovation potential and effectiveness of modern headache care.

PS2-60

Www.ihs-classification.org: the website of the international headache classification

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Background and aims: After publishing the second edition of the international headache classification (ICHD-2), a web-based version was developed. The aim was to make the entire classification available online, globally accessible.

Methods: The contents of the classification are presented at www.ihs-classification.org and continuously updated. The main menu includes the manual for using the classification, the primary headaches, the secondary headaches and the cranial neuralgias. A sitemap and a comparison table allow the conversion of IHS into ICD codes and vice versa. A downloads section makes important IHS publications available. A search function can be used to search the entire classification for specific terms.

Results: Doctors across the globe use this website to look up classification criteria. The website offers the possibility of uploading the classification step by step and including it in different languages. So far, English, German and Italian versions are available.

Conclusion: The web-based version of the international headache classification is a modern approach to making the classification widely available, with advantages over print or simple computer file editions. It improves the practical usability and direct application of the headache classification for both clinical medicine and research.

PS2-61

Medication overuse headache (moh) how can we improve the adherence?

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Objective: To analyze the adherence of MOH patients using two schemes of follow up.

Background: The level of compliance in different chronic disease constitute a challenge. Medication overuse headache has a significant relapse and dropouts risk. A closer monitoring of these patients may contribute to a better outcome. The present study was a part of the COMOESTAS project funded by the European Union.

Methods: 131 Patients with MOH were studied in FLENI pain clinic during two years. The basic method applies was to interrupted the drug in abuse, start a preventive treatment and a rescue therapy if necessary. One group of patients complete a paper diary to identify types and frequency of headache; the other group use a Interactive Electronic Patient’s Record (IEPR) diary to report their symptoms. The follow up was finishes at the 6 months period after detoxification.

Result: We included 77 patients in classic arm and 54 in IEPR. 49 % of patients in the classic approach and 75% in the electronic group finished the follow up.

Conclusion: The use of electronic diary and interactive systems of COMOESTAS project let us a better way to control our patients.

PS2-62

Personality and eating attitudes in idiopathic intracranial hypertension

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Idiopathic intracranial hypertension (IIH) is defined as increased intracranial pressure in the absence of an intracranial mass or hydrocephalus.

It is most frequent in obese women of childbearing age. Observations have led to speculations of hypothalamic-pituitary disturbances in patients with IIH, but conventional tests of endocrine functions have disclosed only inconsistent and insignificant abnormalities in their function.
Weight loss should be recommended for every obese patient, but weight control and guidance by a dietitian often fail and the respective patients don’t loose weight.

Our hypothesis is that these patients suffer from personality disorders with compulsory characteristics and addiction to food. Due to those disorders they are not able to lose weight although they know that their overweight causes them serious health problems.

Twenty-five patients with idiopathic intracranial hypertension were included in the study. The objective of the study is to analyze the personality profiles and eating disorders of those patients.

We used MMPI test to evaluate the personality profiles of the patients and the Eating Attitudes Test to evaluate the changes in their eating habits. The findings of the present study show that the patients have depressive and emotionally overwhelmed MMPI profiles and that they constantly fear that the symptoms could reappear. Though 50% of the patients have an addictive attitude towards alimentation and consume great quantities of high-caloric food. In spite of professional support and although they are beware of the high health risk, they are not able to lose weight.

**PS2-63**

**Cluster headaches: association with mood, anxiety disorders and disability**

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Cluster headache is characterized by attacks of strictly unilateral severe pain with orbital, supraorbital or temporal location and autonomic symptoms.

Attacks typically lost 15 to 180 minutes, and usually occur one or several times per day, specially at night.

The pain is very severe and disabling. The patients have difficulties in having a normal life, they don’t sleep well, are often absent in their jobs - some of them even loose their employment - and use with frequency symptomatic and very expensive treatments. The effects for the patient are severe anxiety, disorders in their mood and disabilities. In order to quantify those effects and to determine quantitative measures of their depression and anxiety, we applied the “Hamilton Depression rating Scale” test and the “Hamilton Anxiety Rating Scale” test to 55 cluster headache patients (thereof 37 with episodic form and 18 with chronic form).

Health related quality of life was studied using a generic (SF-36) and a headache specific (MSQ2.1) instrument.

The results were compared with those of age-and sex-matched healthy persons (50 controls).

The results confirmed our hypothesis: episodic cluster headache patients experience the beginning of a cluster with great anxiety. The chronic cluster headache patients show less anxiety because they are used to the headaches. A high percentage has depressive symptomatology, specially for the chronic forms. The degree of disability and the decrease of quality of life are high in both questionnaires, especially for the chronic forms.

**PS2-64**

**Headache - why to treat with pain killer - may be a symptom of underlying depression - treat by addition of antidepressant & psychotherapy**

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Headache is one of the most common complain ... in and around the world ... like fever headache is not a disease but a symptom of some underlying pathology..... sometimes diagnosed & sometimes undiagnosed.

for those undiagnosed cases where all the investigation are with in normal limits & to further details in to the cause of the headache ... either physician does not have time or training does not support art of conversation or more precisely art of listening or more specific not enough trained in carry on conversion into the depth ... to reveal the underlying psychological factors & to diagnose his personality .. which may the main cause of underlying depression & presenting as a headache.

so how about adding anti depressant to the current therapy & abreaction .. one way of psychotherapy ... let him say every thing .. to doctor .. because doctor is considered as Neutral person . In India ..... In this centre 550 patient of headache who were on Pain killer ... the antidepressant with Psychotherapy was added ..along with supportive treatment like iron & multivitamin of good quality ... it was observed that the frequency of use of pain killer medication was reduced to 90 % & thereby side effect of those medicine on kidney was reduced . another observed was that the mood of the patient was improved, Productivity was enhanced, f requnecy & exacerbation of attacks of headache & migrain was 90 % less.
PS2-65

A retrospective study on incidence of chronic forms in a population of young headache sufferers

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Headache is a common symptom in children and adolescence. In this retrospective analysis we interviewed a population of young patients who arrived to our observation between 1998 and 2000, in order to:

1. determine if the first diagnosis was still adequate and
2. if and which percentage of these young patients developed chronic forms (more than 15 days/month) from episodic forms.

The population of patients was heterogeneous as it included tension type headache, migraine without aura, migraine with aura and mixed forms. 177 patients were screened for the follow up interview. 48 not found, 129 patients were found. 97 were contacted and 32 did not accept to complete the interview. A specific questionnaire was performed, with 5 questions, in order to evidence the clinical aspects of their headache form and its evolution. The original diagnosis was confirmed in all the population of patients: 29 migraine without aura, 55 tension type headache, 13 mixed from migraine without aura and tension type headache. At the original interview en years before, 14 referred more than 15 days of headache/month, 83 suffered from episodic forms. At ten-years follow up, 5 patients referred more than 15 days of headache/month. From this retrospective study we cannot conclude that the evolution of episodic forms in young age is necessarily a chronic form in adult as this depends from natural history and individual and emotional characters of patients.

PS2-66

Self-referring special patients in an outpatient headache clinic

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Aims: A headache clinic should establish consensual referral criteria with general practitioners (GP). Considering prevalence of headache syndromes, a headache clinic is supposed to attend self-referring special patients, among hospital staff and relatives. We aim to compare characteristics of standard and special patients and appropriateness of referring according to established criteria in both populations.

Methods: From January 2009 to January 2011, 751 patients were attended in our headache outpatient clinic. 372 (49.5%, 271 women, 101 males) were referred from primary care (Group A), and 72 (9.6%, 55 women, 17 males) were special patients (Group B). We prospectively considered demographic and nosological characteristics of each patient.

Results: 579 and 128 headaches were diagnosed respectively in the 372 Group A and the 72 Group B patients. Migraine was most frequent headache (A: 54.2%, B: 64.8%). There were no significant differences between Groups A and B when considering age (42.7 ± 17.3 vs 38.1 ± 12 years), years from headache onset (12.5 ± 13.3 vs 15.6 ± 11.9), ancillary tests requirement (33.6% vs 30.6%), Headache Impact Test 6 (HIT6) score (56.6 ± 9.1 vs 59.9 ± 8.3) or previous therapy with preventatives (27.1% vs 30.5%). Adequacy of referrals was similar in both groups (A: 71.8% vs B: 76.4%)

Conclusion: Self-referring special patients represent an important amount of assistance in a headache outpatient clinic. Clinical characteristics and hypothetical adequacy to referral criteria are not different from those observed when GP act as gatekeeper

PS2-67

Galeata: one of the first descriptions of chronic migraine in constantine the african’s liber pantegni

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Aim: Aretaeus of Cappadocia and Galen firstly classified headache disorders. Aretaeus considered that heterocrainia (a kind of ancient acute migraine) could lead to a chronic headache, and Galen described cephalae as a chronic headache with paroxysms sometimes accompanying photophobia and phonophobia.

Methods: Constantine the African (1015-1087) translated Arabic medical books into Latin, reintroducing Greek medicine in Medieval Europe and influencing European medical teaching for centuries. Kamil as-sina’a at-tibbiya (“complete book of medical art”), written by the Persian physician Ali ibn Abbas was Constantine’s first translation
to Latin, and his best-known work, Liber Pantegni. We have carried out a descriptive review of Henricum Petrum’s Latin edition, year 1539, paying special attention to headache syndromes descriptions, and attempting to relate them to today’s views on headache.

**Results:** Liber Pantegni contains ten books. One chapter of ninth book is completely dedicated to headaches. Liber Pantegni distinguishes cephalæa, hemicrania and galeata. Cephalæa is a holocranial pain due to systemic diseases or trauma. Hemicrania is caused by meningeal disturbances related to bad humours or slow digestions, sometimes associating loss of vision. Finally, Galeata is described as a chronic headache with occasional exacerbations, quite difficult to treat. When intensity increases, patient does not tolerate light, noise or movements, and searches darkness and quietness. Sometimes, pain may radiate to eyes.

**Conclusion:** Liber Pantegni is considered a pivotal text in the early development of European medicine. It contains one of the first descriptions of chronic migraine, Galeata, independently considered in its headache disorders classification.

**PS2-68**

**Epicrania fugax: a prospective series of 14 new cases**

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**Aim:** Epicrania fugax (EF) is a novel headache syndrome presenting with brief pain paroxysms that always start in a fixed posterior cranial region and suddenly spread forward to the ipsilateral anterior scalp. Pain may be accompanied by ipsilateral autonomic symptoms. We aimed to analyze the demographic and clinical features of 14 new cases.

**Methods:** From January 2010 to January 2011, 14 patients with EF (7 male, 7 female) were attended at the headache clinics of two tertiary hospitals.

**Results:** Mean age at onset was 44.3 years (SD: 18.3, range: 27-82). 12 patients had strictly unilateral pain, while 2 patients had side-shifting. The pain started in occipital (n=11), parietal (n=2), or parieto-occipital (n=1) regions. 8 patients reported a dull interictal pain in the stemming point. Pain irradiation followed a linear (n=13) or zigzag (n=1) trajectory, reaching the eye or the forehead (7 cases each). Pain quality was mainly described as electric, and pain intensity was rated as 6.5 ± 0.6 (range: 3-10) on a 10-point visual analogue scale. The complete sequence was very brief (usually < 5 sec), and the frequency was quite variable. 4 patients identified triggers, and 5 had autonomic features. Prophylactic therapy was prescribed in 11 cases. Gabapentin, lamotrigine or occipital nerve blocks achieved complete resolution in some of our patients (4, 2 and 1, respectively)

**Conclusion:** This new series reinforces the proposal of EF as a new headache syndrome. Nerve blocks, gabapentin or lamotrigine may be helpful for individual patients. Further observations and therapeutic trials are needed.

**PS2-69**

**Effects of botulinum toxin-a on anxiety and depression levels in patients with cervicogenic headache**

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**Introduction:** First Cervicogenic headache patients were reported by Sjaastad in 1983. It’s prevalence is between 0.4-2.5% in population. There have been no studies evaluating the effects of BTX-A on anxiety, depression levels in patients with cervicogenic headache. This study aimed to determine the effects of BTX-A on anxiety, pain frequency, anxiety and depression levels in patients with cervicogenic headache.

**Materials and methods:** 22 patients who had headache on cervicogenic region were enrolled. Each patient was injected by totally 150 units of Dysport. Patients were followed for 6 weeks, pain severity was recorded by Visual Analog Scale (VAS) and pain frequency were also recorded. Beck anxiety, Back depression scales were also performed to participants.

**Results:** While pain frequency was 19.72±5.71 at baseline, it had decreased to 7.60±4.19 after treatment. VAS levels had decreased from 79.70±10.20 to 45.60±17.25 after 6 weeks. Beck anxiety scores had decreased from 31.80±10.44 to 13.48±8.38 and Beck depression scores had decreased from 10.60±3.95 to 8.70±5.01 after 6 weeks.

**Discussion:** According to our results BTX-A application had decreased pain severity, pain frequency and anxiety levels. But depression levels didn’t change. We have determined significant decrease in anxiety symptoms. BTX-A
may have anxiolitic effects and analgesic effects by inhibition of neurotransmitters and neuropeptids.

Only few studies reported BTX-A efficacy on cervicogenic headache but they had not determined the effects on anxiety and depression. Further studies with larger patient population with control groups are necessary to determine BTX-A effects on anxiety and depression in patients with cervicogenic headache.

PS2-70

The efficacy of local lidocaine injection in patients with frequent episodic tension-type headache: a randomized, placebo-controlled double-blind clinical trial

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The aim of our study was to evaluate the efficacy of local lidocaine injection into the myofascial trigger points (TP) in pericranial muscles to regulate the antinociceptive system at the treatment of frequent episodic tension-type headache (ETTH).

Materials and methods: 36 patients that were diagnosed with frequent ETTH, aged between 18-65 years were included in the study. Pain severity was evaluated using the visual analogue scale (VAS) and painful days per month were recorded. Patients were randomly divided into 3 groups. Group 1 (n = 12) received 1 saline (NaCl 0.9%) injection and group 2 (n = 12) received 1 lidocaine (0.5%) injection. Group 3 (n = 12) received 5 injections of 2ml lidocaine (0.5%) on alternate days. The efficacy of the injections were evaluated 2, 4, and 6 months after treatment.

Results: No differences were observed between group 1 and group 2. Group 3 had better scores than group 1 after treatment, both in terms of painful days per month and VAS score (P < 0.05). Additionally, improvement in group 3 was statistically significant (both in terms of painful days per month and VAS score) post treatment (P < 0.05).

Discussion: 5 injections of lidocaine (0.5%) on alternate days are suggested for patients with frequent ETTH, which provide long-term pain relief in our study. Our treatment protocol might also be a promising treatment of choice for primary headache disorders. Additional placebo-controlled studies that with larger study populations are needed to confirm our results.

PS2-71

The relationship of anxiety and depression levels with alexithymia in patients with migraine and frequent episodic tension type headache

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Introduction: Psychiatric comorbidity is commonly seen in patients with headache disorders. Studies have shown increased anxiety and depression in patients with migraine and tension type headache. However, the relationship of anxiety and depression levels in patients with headache disorders has also been studied. The aim of our study was to reveal the relationship of anxiety and depression levels with alexithymia in patients with migraine and frequent episodic tension type headache (FETTH).

Patients and methods: Patients with migraine (n=29) and with FETTH (n=32) formed the study groups, 30 healthy individuals formed the control group. Beck Depression Inventory, Beck Anxiety Inventory and Toronto Alexithymia Scale were applied to subjects. Disease characteristics (duration of disease, painful days in a month, headache attacks in a month) of the patients were also recorded. The relationship of anxiety and depression levels of each group with alexithymia and disease characteristics were evaluated.

Results: Alexithymia, depression, anxiety levels in FETTH group was significantly higher than control group. Anxiety levels of migrain group were higher than control group. Proportion of alexithymic individuals in FETTH group was higher than migraine and control groups. In FETTH groups, depression and anxiety levels of alexithymic individuals were higher than non-alexithymic individuals.

Discussion: Our results confirmed that alexithymia levels of patients with FETTH was higher than migraine and control groups. And this condition was closely related with depression and anxiety levels of the patients. Our results may also suggest that different pathopsychological processes may play a role in the development of FETTH and migraine.
PS2-72
Secondary cough headache due to Arnold Chiari type-1 malformation: case report
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Introduction: 40% of the cough headaches is symptomatic and Arnold Chiari type-1 malformation is mostly detected in these group. This current report demonstrates a secondary cough headache due to Arnold Chiari Type-1 malformation.

Case: A girl, aged 14, has been suffering from a moderate pulsatile headache starting from her neck and spreading to all over her head and lasting in 3-5 minutes for the last 6 months. Her headache attacks can be provoked by repeated cough, sustained laughing or crying, blowing her nose too hard. Nausea also accompanied to her complaints. Her neurological examination was normal. Her brain MRI scan revealed Type-1 Chiari malformation. In order to trigger her headache attack, she was asked to make repetitive valsalva maneuvers duration of each was 5 seconds. Her headache attack was triggered during the fifth valsalva maneuver. Patient was diagnosed as secondary cough headache due to Arnold Chiari Type-1 malformation.

Discussion: Secondary cough headache due to Arnold Chiari Type-1 malformation can be prevented safely by some precautions which prevent increase in the intracranial pressure.

PS2-73
Cough headache may be a result and a cause: case report
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Objective: Chronic cough is a symptom that lasts more than three weeks. The receptors of cough reflex exist in many organs. Vagal branches make up afferent path of the reflex. Trigeminal, glassofarengeal, phrenic nerves play a role in the transmission of impulses to the reflex center. Voluntary control of cough is governed by cerebral cortex, and reflex control by the reflex center in medulla oblongata. Efferent path is made of phrenic nerve, spinal motor nerves, recurrent laryngeal branch of vagus. In this report, a case who had headache due to cough was discussed.

Case: 52 year old male patient applied to our clinic with severe headache, throbbing style on both sides of his head, by just having coughed for four months. Headaches after cough lasted about 10 seconds. Neurological examination, imaging, BOS pressure was normal. Indomethacin, ase佐tozal, topiramate treatments were not effective. We determined that the patient was using an ACE inhibitor for hypertension. When drug was ceased, cough symptoms disappeared within a month, decreasing from the first week.

Results: Chronic cough can occur with the use of ACE inhibitors. The mechanism of cough formation is unclear, however inflammatory mediators such as bradykinin are thought to be responsible. Headache is reported to be due to the pain-sensitive structures strained by increased intracranial pressure during cough. In our case, it appears that cough is due to the use of ACE inhibitor, while the headache is the result of cough. Cough and headache disappeared after the drug was stopped, that confirmed the diagnose.

PS2-74
High prevalence of headache syndromes in chronic pain patients
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The prevalence of chronic pain in Switzerland is estimated to be 16% in the general population. The prevalence of chronic daily headache is about 3%. We investigated the prevalence of headaches in patients who were referred for pain other than headaches to the pain clinic of our tertiary care pain centre.

During a 12-month-period all 769 patients who were referred to our pain clinic (and not to our specialized headache clinic) were screened for headaches by a pain specialized physician. All patients with headache (18,3%) were then seen by a Neurologist and had a standardized headache interview. Diagnoses were made according to ICHD-II criteria. The diagnoses were: migraine 41,8%, frequent episodic tension type headache 19,9%, chronic tension type headache 19,1%, posttraumatic headache 7,1%, medication overuse headache 26,2%, headache due to
temporo-mandibular joint disorder 15.6%. In 35.5% of all patients headache was the most troubling complaint. Although being referred to a general pain clinic, 11.3% had headache only, [s1] 18.4% had 1 additional pain side and 70.2% had 2 and more additional pain sides like shoulder, arm, back and leg pain.

According to SF12 quality of life was low (mean physical score 31.1, SD 9.0; mean psychological score 38.1, SD 10.5). [s2] 81.4% of patients had CPGQ stadium III and IV. 62.8% of patients had borderline or abnormal HADS depression subscores.

We conclude that there is a high prevalence of headaches in chronic pain patients suggesting possible comorbidity. This might have diagnostic and therapeutic implications, but needs to be confirmed.

**PS2-75**

**The effectiveness of cognitive-behavioural therapy for post-traumatic headaches**

**B. Gurr**: Head Injury Patients

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Post-traumatic headache is one of the most common symptoms following mild and moderate head injury. Psychological factors are believed to play a role in the cause, maintenance and relief from chronic post-traumatic headache. This research evaluated the effectiveness of a multi-dimensional cognitive-behavioural approach towards rehabilitation of post-traumatic headaches.

The sample included 20 participants with post-traumatic headaches from an original sample of 41. Participants acted as their own controls. Outcome measures consisted of self-rating questionnaires to assess headache severity, intensity, duration, functioning and emotional well-being. Emotional and functional headache characteristics were studied using a multi-dimensional investigation which included relatives’ perceptions of the sufferer’s headaches. The intervention proved effective and beneficial for the 20 therapy participants. It is concluded that cognitive-behavioural therapy provides a useful supplement to the treatment of post-traumatic headache.

**PS2-76**

**Cluster headache attack cessation and remission extension of months or longer in six treatment-refractory patients administered only 3 doses of bol-148**

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Five male patients with treatment-refractory chronic cluster headache and one female patient with treatment-refractory mixed cluster/migrainous headache were administered 2-bromo-LSD (BOL-148) (20mcg/kg) at five-day intervals for a total of three treatments. Sixteen-week outcome data on the five male patients revealed a robust treatment response, with three of the five having no attacks for more than one month, thereby shifting their diagnosis back to the episodic form of cluster headache. Similarly, the female patient reported quiescence of cluster attacks for greater than one month and "significant" improvement in migraine in the following weeks from last dose of BOL-148. This poster presents longterm outcome data on all 6 patients who received BOL-148. In follow-up with these patients, BOL-148 provided significant headache relief that lasted for several months to more than one-year. Data suggests that BOL-148 may function as an important new treatment, though, at present, there is no expansion for such long-term prophylactic effects with no later drug re-administrations. There is some evidence that BOL-148 is affecting epigenetic mechanisms and may open the possibility for a near-cure-like treatment for patients afflicted with vascular headaches.

**PS2-77**

**Association of migraine and right-to-left-shunt? A population-based study**

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**Aim:** To investigate prevalence of a right to left shunt (RLF) in a population based sample of migraine with aura (MIG-A), migraine without aura (MIG) and controls (C).

**Background:** An association between RLF and migraine with aura was reported in many case control studies, which however recruited patients through tertiary headache centres and might therefore suffer from a substantial selection and investigator bias.

**Methods:** Current case control study was nested into the large (N=18,000) population based German Headache Study. Six thousand people were screened for primary headaches in the city of Essen, of whom

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3336 responded (56%). All patients with MIG-A, a random age and gender matched sample of respondents with MIG and another matched sample of people without headache were invited transcranial Doppler examination (bubble test).

**Results:** After telephone interview and neurological examination we were able to recruit 42 MIG-A (33 females, mean age 49.6 ± 10.4 y), 44 MIG (32 females, mean age 49.6 ± 11.3) and 32 controls (24 female, mean age 48.8 ± 8.7).

RLS was found in 45.2% (19/42) of respondents with MIG-A, in 34.1% (15/44) of respondents with MIG and 37.5% (12/32) controls (p = 0.562, Kruskal Wallis Test).

**Conclusion:** We conclude that there might be a higher RLS prevalence in MIG-A, although the observed difference of about 10% between the different groups was statistically not significant. Despite the large initial sample size we were not able to achieve enough power, which requires about 700 participants per group and stretches this study beyond its limits.

**PS2-78**
**Headache secondary to lead poisoning after taking Chinese herbal pills: a case report**

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**Objective:** To report an adult case of headache secondary to lead poisoning after taking Chinese herbal pills.

**Background:** Traditional Chinese medicine (TCM), including herbal therapy and nutritional support, is popular in China and Taiwan. TCM have been reported to contain heavy metal such as lead and cause lead encephalopathy in young children. But in adult, such case was rarely reported in the literature.

**Method:** A case report.

**Results:** A 51-year-old woman presented with acute progressive bi-frontal headache, accompanied by nausea, blurred vision, and diplopia for 2 weeks. She also complained dizziness, memory loss, irritable mood, and ataxia. Physical exam revealed bilateral disc edema. Routine blood tests showed severe anemia. Magnetic resonance images showed high signal intensities of left parietal and bilateral frontal lobes in T2-weighted and fluid-attenuated inverse recovery images. The results of lumbar puncture were remarkable for high intracranial pressure (280 mmH2O) and concentration of total protein (145 mg/dl). Her blood lead level is as high as 137.6 μg/dl, attributable to the contaminated Chinese herbal pills she consumed (lead concentration: 17,504 ppm). Her headache and all other symptoms improved markedly after several courses of chelating therapy.

**Conclusion:** Our patient fulfilled the diagnostic criteria of lead encephalopathy, and also headache attributed to intracranial hypertension secondary to toxic causes (International Classification of Headache Disorders, 2nd edition: 7.1.2). Since headache secondary to heavy metals is potentially treatable. This case reminds us the importance of querying medication history, including any traditional or complementary medicine, while approaching patients with headache.

**PS2-79**
**Spontaneous vertebral artery dissection with thunderclap headache complicated medullary infarction in a young female**

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**Background:** Headache is the most common, initial, and even isolated symptom in patient with cervical artery dissection. It usually occurred gradually, however, sudden onset as thunderclap headache was noted occasionally.

**Case report:** We presented a 44-year-old female experienced sudden onset severe right side nuchal pain and vertigo while quietly sitting on a chair. The pain radiated to right posterior occipital region minutes later, followed by nausea and vomiting. She denied visual problem, tinnitus, facial pain, dysarthria, or focal limbs weakness. On exam, her right occipitonuchal region was exquisitely tender to palpation. The other physical and neurological exams are unremarkable. On day 2, her headache and vertigo were much better, but her trunk was deviated to right side. Brain magnetic resonance imaging showed faint hyperdensity lesion at right upper medulla in diffuse weight image, but brain angiography was normal. Further cervical computed tomography angiography showed right vertebral artery dissection. Aspirin 100mg per day was prescribed, and her truncal deviation was improved quickly 2-3 days later. Her headache and vertigo was completely gone at day 7.
Conclusion: Cervical artery dissection could present with isolated thunderclap headache and delayed stroke. Early initiation of antplatelet or anticoagulant drugs after urgent and correct diagnosis could possibly prevent further complicated stroke. Headache with obvious vertigo and neck pain may offer a hint to the quick diagnosis of cervical artery dissection.

PS2-80

Atlas of headache disorders and resources in the world. A survey by the world health organization and LIFTING THE BURDEN: the global campaign against headache

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Background: Headache disorders are prevalent, disabling and costly, and should be a public-health priority.

Aim: This global enquiry, in WHO’s Atlas series, documents headache-related health-care needs and provision.

Methods: Questionnaires were sent to neurologist, GP and lay respondents in WHO Member States, grouped into WHO regions and World Bank income categories.

Results: Questionnaires returned from 101 countries and all regions represented 86% of the world’s population, half to three-quarters of whom have had headache in the last year (>10% have migraine, and 1.7-4% have headache on ≥15 days/month). Worldwide, scarce information exists on the societal impact of headache disorders (18% of respondents); they are seldom included in annual health reporting systems (12%) or national expenditure surveys (7%). Only 10-40% of people with headache are professionally diagnosed. ICHD criteria are used in 56% of countries, fewer in low-income countries. Investigation rates are generally high, more than expected for disorders that mostly do not require investigations. Half of people with headache are self-treating, while 10% are treated by neurologists (fewer in lower-income countries). Management guidelines are in routine use in 55% of countries. Few hours are committed to headache in undergraduate (4 hr) and specialist medical (10 hr) training. The major issues reported in lower-income countries focus on lack of health resources generally, whilst higher-income countries report lack of headache-specific resources.

Conclusions: Headache disorders receive low priority, or are ignored. Health-care systems underuse primary care and overuse specialist care. Training is manifestly inadequate. Remedial action requires political recognition that these problems exist.

PS2-81

Pilot study migraine care for knowledge spreading on migraine diagnosis and therapy in the calabria region

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Introduction: Statistical data on the incidence of migraine syndromes in Calabria overlap with the data in the international literature; however, the lack of an informative, training, diagnostic and clinical network surely does not allow researchers to identify “treatment protocols” to tackle the problem globally, thereby being an hindrance to a more qualified medical care and to a more comprehensive approach in the management of migraine patient.

Aims: Within this perspective, and within a limited time-span of activity (about three months), the aims of the initiative are the following: to develop a communication campaign in order to establish several new contacts; to increase patients’ access to the “territorial outpatient nursing management system”; to foster the application of a “managerial” medical model within the public healthcare system.

Materials and methods: Hypotheses of activities include the use of media communication instruments, through which the concept should become widespread, i.e. communication campaign through “posters”; newsletters sent through e-mail marketing; organisation of events awarding CME credits; development and administration of an ad-hoc questionnaire to patients with a section devoted to the assessment of the communication campaign; and a tailor-made questionnaire for the “stakeholders working in the territorial outpatients nursing management network”.

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Conclusion: In terms of the planning of an awareness campaign, outlining the differences between the marketing and social communication campaign is useless, since communication strategies and techniques are identical and, moreover, it is fundamental to spread correct information and to foster the application of decision-making algorithms aiming at the best clinical practice.

PS2-82

Anxiety, depression, stress and migraine

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Objective: Anxiety and Depression are often underlined as triggering factors in migraine. General study have found a link between migraine and psychiatric comorbidities, especially anxiety and depression.

Material and method: Our study took place in the Center for Headache Study on Adaptative Disorders. for migrainous patients and model management health day service headache. HIS criteria were used in order to confirm diagnoses. The control group had never suffered from headache before. Both patients and control were 2 questionnaire: Hospital Anxiety on Depression Scale (15 items) and the perceived Stress questionnaire (10 items). Differences among groups were found in most of the tests evaluating anxiety, depression on stress. For all items except for depression in men \( p < 0.001 \). The significant level clinical Depression on Anxiety is score \( >12 \). According to the perceived stress scale, it should be score \( >8 \). The physical examination includes: inspection, emotional and neurological status.

Results: 62 patients consecutively in the day service headache between september 2010-february 2001 were studied (38 F 24 M), first visit center was 35.8 years, 33.1 years for males and 36.7 years for females; when compared to the control, patients migraine presented high levels of neurotism, extraversion, and external locus of control.

Conclusion: Intensity of anxious disorders and the level of perceived stress were higher in the migrainous group compared to the control from statistical and clinical point of view.

PS2-83

A headache clinic for 5 years in an urban city of Japan

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Objective: The author evaluated all patients attending a headache clinic over 5 years: how they found out about the clinic, types of headache and previous medication.

Subjects and methods: All patients completed questionnaires, including the Headache Impact Test (HIT6), and were interviewed by the author. Headache diagnosis was based on ICHD-2.

Results: Of 2742 patients (655 men and 2087 women, 6-93 years old) attending the clinic during 5 years. 33% found the clinic by an internet search, 17% by media such as TV, newspaper and magazine, 14% were referred by a doctor, and 14% were recommended by an acquaintance. The average HIT6 for all patients was 63.4 ±7.2. At the first visit, 1472 patients (311 men and 1161 women) were diagnosed with migraine, 284 (41 men and 243 women) with migraine and tension-type headache (TTH), 288 (113 men and 175 women) with TTH and 399 (67 men and 332 women) with MOH. The percentage of the patients with migraine decreased with increasing age. The percentage with MOH was constant from teens to 60s. 61.4% of migraine patients had previously visited another doctor, compared to 81.8% with chronic TTH and 78% with MOH. Among 1078 patients with migraine who had visited a doctor before, 414 (38.4%) had taken triptans; only 109 (10.1%) had taken prophylactic medication.

Conclusions: Half the patients found out about the clinic from the internet or media. Headaches had a severe impact on the quality of life of all the patients, who need appropriate information and medication.

PS2-84

Medication overuse headache: rates and predictors for relapse in a 5-year prospective study

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Introduction: Preventive medication for primary headache is important to prevent relapse of medication overuse headache. However, the period and frequency of long-term preventive medication have not been fully investigated. This study aimed to clarify the period and frequency of long-term preventive medication for patients with successful withdrawal treatment for medication overuse headache and examine the presence of any features
associated with medication overuse headache based on the medication being overused.

Methods/patients: This prospective 5-year follow-up study included 39 patients with medication overuse headache. Follow-up interviews were performed face-to-face or by telephone. Type of overused medication, duration between withdrawal and repeated overuse, and follow-up status were investigated in patients with relapse.

Results: Follow-up data were available from 26 patients (72.2%). Of these patients, 19% relapsed, 35% were free from preventive medications, and 43% were receiving preventive medications. All male patients (n=3) were free from preventive medications; 52% of female patients (n=12) were receiving preventive medications (P=0.0406; χ² test). Four of 5 relapsed patients had relapsed after self-withdrawal of preventive medications.

Discussion/conclusion: Our findings suggest that medication overuse headache patients, especially women, need continuous preventive medications for many years after withdrawal to prevent relapse.

PS2-85
Ophthalmic pitfalls for headache specialists
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There is considerable overlap in the pain phenotypes associated with some primary headache syndromes and some primary ocular pathologies, providing fertile ground for misdiagnosis. Some ocular pathologies are difficult to diagnose without specialist equipment and examination techniques. From an ophthalmic perspective we explore a number of benign and potentially sight threatening ocular pathologies which can easily masquerade as primary headaches. We aim to raise awareness of a number of such ophthalmic conditions and provide, where possible, a practical approach to help practitioners without ophthalmic training eliminate them from the differential diagnosis. The discussion includes scleritis (particularly posterior scleritis), uveitis, recurrent corneal erosion syndrome, intermittent angle closure glaucoma, orbital pseudotumour, giant cell arteritis, ophthalmic shingles and zoster sine herpete.

PS2-86
Sunct in Japanese - a case report and review of literature in Japan
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Background: Short lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is seldom reported in the East Asia including Japan.

Subject and methods: We have experienced one Japanese SUNCT patient and also reviewed SUNCT cases reported in Japan.

Case report: A 29-year-old man presented with sudden-onset intermittent left-sided orbital headache, which was not accompany by lacrimation and conjunctival injection. We diagnosed trigeminal neuralgia at first and administered carbamazepine and loxoprofen. However, these medications were entirely ineffective at all and 6 days later, autonomic symptoms including conjunctival injection and tearing appeared. Diagnosis of SUNCT was made and gabapentin was started at up to 800 mg per day. Soon after, the headache and autonomic symptoms disappeared. Gabapentin at 800 mg per day was continued for 3 months and then reduced to 400 mg per day. Soon he had only a slight headache without tearing and conjunctival injection. He has continued to take gabapentin at 400 mg per day until now.

Result: Only 8 cases including our case have been reported in Japan. Clinical course, treatments are diverse.

Conclusion: Our case indicated that headache and autonomic symptoms in SUNCT did not always emerge simultaneously, but they sometimes appear with time lag. The incidence of SUNCT may be higher than expected, suspecting that this disease may be underestimated or misdiagnosed in the East Asia including Japan. A therapeutic strategy and optimal dosage of medications should be established for the treatment of SUNCT.

PS2-87
Naratriptan in prophylactic treatment of cluster headache: case reports of seven patients
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Introduction: Naratriptan, 5-hydroxytryptamine1B/D (5-HT1B/D)-agonist, is an effective medicine for migraine. Naratriptan has also been reported to reduce the
frequency of cluster headache (1-3). The purpose of this study is to determine whether naratriptan would show efficacy in prophylactic treatment of cluster headache in Japan.

Methods: We report seven patients with cluster headache preventedly treated with naratriptan. We used the International Classification of Headache Disorders; 2nd Edition (ICHD-II) for diagnosing of cluster headache. The study was conducted in three centers (Department of Neurology, Saitama Medical University, and Saitama Neuropsychiatric Institute, Saitama International Headache Center) and patients were recruited from these specialized headache outpatient centers. Naratriptan was taken before they went to bed.

Results: Five of the seven patients with cluster headache have shown no attack after naratriptan treatment. In one case, the frequency of attacks was decreased by naratriptan. But naratriptan had no effect for her headache in one case.


PS2-88
Gender differences in pain perception and depression in migraine patients
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Background and aims: Migraine attacks are characterized by moderate to severe pain which may influence patient’s emotional status. In individual patients depressive reactions are expected to be influenced by the severity of migraine pain. The aim of our study was to compare perception of pain and level of depression between male and female migraine patients.

Methods: We surveyed a total of 89 age-matched migraine outpatients (57 females and 32 males). The intensity of depression was assessed by the Beck Depression Inventory (BDI) and the perception of average pain intensity in a migraine attack was displayed by the Visual Analogue Scale (VAS).

Results: The results on VAS showed that 70% of female patients reported severe intensity of pain (by scores 8-10) while males equally distributed scores for moderate (4-7) and severe intensity of pain. On the other hand female patients were less depressed than male patients on BDI (t=3.6, p<0.01).

Conclusion: We conclude that gender differences in perception of pain intensity in migraine attacks do not appear to be a major contributing factor to the level of depression in migraineurs.

PS2-89
Prevalence of headache in school-children and impact of socioeconomic factors. Hbsc study, lithuania
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Background: This study is the first survey of headache in schoolchildren in Lithuania. Numbers about headache prevalence do not exist for Eastern Europe.

Objective: To determine the prevalence rate of headache in 11-15age children and the role of possible related SES-factors. This study is a part of the Cross-National Survey on Health Behavior in School Age Children - WHO Collaborative Study (HBSC).

Methods: The standardized HBSC(Lithuanian version) questionnaire was administered to 5632 schoolchildren in 2005-2006. Totally 2904 (51.6%) boys and 2728 (48.4%) girls were enrolled. The average age - 13.0±0.1yr. The responce rate - 86%. The evaluation of an impact of SES-factors was based on this items: parent’s education and occupation, family income and structure. Lithuania belongs to upper- middle-income economies country.

Results: The overall prevalence of frequent headache (at least once/week) was 24.2% and 42.7% (at least once/month) (χ²=131;df=8;p<0.001). Boys are less at risk than girls (χ²=206;df=4; p<0.001) and the prevalence increases with age (χ²=56.8;df=2;p<0.001). The vast majority of respondents, suffering from headache, their subjective health assessing as good (χ²=72.9;df=1;p<0.001). Family income had a strong association with adolescent’s headaches and significantly more prevalent among girls from low income families (χ²=13.4;df=2;p=0.01). Adolescents who lived in two-parent families and had good relationships with their parents experienced less headache cases (χ²=19.5;df=3;p<0.001).
**Conclusion:** School age, especially in adolescence, family richness and structure had a great significance on the prevalence of adolescent’s headache and should be considered when thinking about treatment.

**PS2-90**

**Folk remedies for headache among turkmen people in northern iran: micro-medical ethnographical study**

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**Background:** Experiences and information that pass from generation to generation by oral transmission contain a variety of home remedies. Since, there are different ethnic groups in Iran, a broad spectrum of folk medicine experiences and health beliefs exist. Turkmen are one of the major ethnic groups in Northern Iran, Golestan province. The aim of this study was to explore the traditional remedies for headache in among Turkmen people.

**Methods:** Semi-structured interviews were conducted with the healers and older adults who have had experiences with using folk remedies. All of the interviews were transcribed line by line. The data were coded, categorized and described.

**Results:** The informants mentioned to a variety of herbal plants and home procedures. To make better the pain of headache due to hypertension the special tea of Boraginaceae and lemon and candy was prescribed. The headache of tension was treated by Sweet violet tea and candy or steam of Chamomile. In case of migraine headache, using bitter almond oil, the head will be rubbed. To relief the headache due to injuries, some yolk egg and Harmal will put on the head. To relief headache of typhoid a blend of lemon juice, pomegranate sausage, yoghurt and wheat flour will put on center of skull.

**Conclusions:** Health care providers should be aware of these remedies, to educate people about remedies that may be harmful. Most remedies used pose no threat to health. In some cases, remedies may be blended with traditional medical treatments to ensure better patient compliance.

**PS2-91**

**Restless legs syndrome as a comorbidity of migraine**

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**Background and aims:** Migraine is known to be comorbid with a variety of other neurological disorders. Restless legs syndrome (RLS) is one of them. RLS is a disorder of restlessness associated with discomfort in the legs and arms. The restlessness is relived by moving the limbs and worsened by rest. We studied what population of our outpatients who visited our headache clinic had RLS.

**Methods:** We conducted a survey with all the outpatients who visited our headache clinic, which was located in the center of Osaka, the second largest city of Japan, from December 2010 to January 2011. By handing out a questionnaire, we picked up all the RLS suspected patients.

**Results:** The number of the outpatients was 255 in total. 52 patients were suspected to have RLS. The prevalence was 20.39%. Among them, 164 patients had migraine without aura (MO), and 32 of MO patients were suspected to have RLS (19.51%). 24 of the outpatients had migraine with aura (MA), and 8 of MA patients were suspected to have RLS (33.33%). 67 of the outpatients had other headache disorders and 12 of them were suspected to have RLS(17.91%).

**Conclusions:** The migraine patients had a significantly high prevalence of suspected RLS, and especially MA patients were strongly associated with suspected RLS.

**PS2-92**

**Submandibular gland carcinoma presenting with trigeminal neuralgia: case report**

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**Introduction:** Symptomatic trigeminal neuralgia (STN) itself may sometimes occurs alone, before it’s underlying cause becomes evident. This current case demonstrates a submandibular gland carcinoma as an initial symptom of STN.

**Case:** A man (aged 61) has been suffering from an electric-shock-like pain attacks with a sudden onset, emerging from his right lower mandible, spreading to right side of his head for the last 6 months. When his complaints began, the frequency of these attacks were on alternate days and increased to 2-4 times a day for the last 4 weeks. His neurological examination revealed trigger points at the
area innervated by maxillary and mandibular branches of the trigeminal nerve. His pain can also be triggered by percussion of the right upper, right lower molars. Brain MRI and paranasal sinus computed tomography of the patient were reported normal. Pregabalin (600 mg/day) treatment was given. During the follow-up patient's complaints persisted and a mass lesion located at the right submandibular region was detected. Patient was diagnosed as submandibular gland carcinoma according to positron emission tomography and biopsy results. He underwent surgery and chemotherapy. Pregabalin treatment was continued for 3 months after the surgery. Pain attacks was decreased during the 3 months follow-up and resolved completely.

**Conclusion:** This case suggest that of trigeminal neuralgia which arises from the mandibular branch of the trigeminal nerve may be an indicator for any lesion of perimandibular region. Patients who are resistant to medical treatment for trigeminal neuralgia must be investigated for early diagnose of mass lesions.

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**PS2-93**

Nocturnal headache related with melatonin deficiency due to a pineal gland cyst: case report

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**Background:** Cyclic characteristics of some of the headache disorders are closely related with melatonin which is secreted by the pineal gland.

**Case:** A man, aged 29, has complained with headache attacks awakening him in the middle of the night and lasting until mornings for the last 2.5 years. These headache attacks were pulsatile and continued until the sunrise. During these attacks, he also suffered from allodynia over the scalp, bilateral conjunctival hyperemia and nervousness. A neuroepithelial cyst 5x4 mm in size has been detected in the pineal gland in his brain MRI. The peak serum melatonin level that was measured at 02:00 am was 28 pg/ml.

**Results:** He underwent oral melatonin treatment with a dosage of 6 mg/day. After a month, he relieved 70% of his complaints. When the dosage of melatonin was increased to 10 mg/day, he became headache-free and had no complaints five months after the treatment. His control serum melatonin level at 02:00 am was 61 pg/ml.

**Conclusions:** To our knowledge, this is the first headache case that occured only at midnights in relation with low melatonin level due to a neuroepithelial cyst in the pineal gland.

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**PS2-94**

Efficiency of melatonin in chronic tension type headache patients and effects on anxiety and depression

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**Instruction:** Tension type headache (TTH) which is a primer headache, has episodic and chronic forms. Peripheral and central nociceptive mechanism are thought to be responsible in occurrence of chronic TTH. Psychiatric disorders are frequently associated with chronic TTH. Although basic and combined analgesics are used in acute treatment and antidepressants are used in prophylaxis, we need new treatment modalities. In this study we aimed to determine the efficacy of melatonin use in chronic tension type headache patients and effects of it on anxiety and depression.

**Materials and method:** 21 chronic TTH patients were included in this study. 3 mg/day melatonin were ordered to each patients during 3 months. Painy days in a month, severity of pain (by using Visual Analog Scale (VAS)), Hamilton depression scores and Hamilton anxiety scores were detected before and 3 months after the treatment.

**Results:** 5 men and 16 women were included in this study. Mean age of patients was 33.14±8.95 (19-51) years. Painy days in a months decreased from 20.14±4.00 days to 13.76±3.14, VAS scores decreased from 65.95±11.46 to 50.95±13.28, Hamilton depression score decreased from 21.23±7.54 to 15.76±5.55 and Hamilton anxiety scores decreased from 16.66±8.71 to 11.80±6.42. Developments in all parameters were statically significant (p<0.05).

**Conclusion:** Our results indicates that melatonin should be used as an efficient and safe treatment method in chronic TTH.

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PS2-95
Botulinum neuro-toxin type-a in the treatment of chronic tension type headache associated with pericranial tenderness
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Introduction: Both peripheral and central nociceptive mechanisms are responsible in chronic TTH. Analgeics are used in the acute treatment of chronic TTH and antidepressants are used in prophylactic treatment. However, further studies are needed to bring out new treatment options. The aim of our study is to investigate the effectiveness of Botulinum Neuro-toxin Type-A (BoNTA) in the treatment of chronic TTH associated with pericranial tenderness (PT).

Materials and methods: 14 patients with chronic TTH with PT were included in the study. 50 units Botox injection was applied to the pericranial muscles (5 units for each muscles bilaterally: frontal, temporal, semispinalis capitis, spenius capitis and trapezius muscles) for each patient. Severity of headache was evaluated by VAS (Visual Analogue Scale) and number of days with headache per month were recorded before treatment and 2nd and 4th months after treatment.

Findings: Number of days with headache per month were 19.57 ±3.25 before treatment, 15.28 ±4.37 at the 2nd month after treatment and 15.78 ±3.90 at the 4th month after treatment. Severity of headache was 65.71 ±9.16 before the treatment, 50.71 ±13.56 at the 2nd month after treatment and 54.28 ±10.35 at the 4th month after treatment (p< 0.05). Frequency and severity of headache before treatment were significantly decreased at the 2nd month after treatment and this significance continued at the 4th month after treatment (p< 0.05).

Result: BoNTA treatment may be usefull in the treatment of patients with chronic TTH associated with PT.

PS2-96
Efficacy of local lidocain application on anxiety and depression and its curative effect in patients with chronic tension type headache
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Central and peripheral nociceptive mechanisms have been suggested in the development of chronic tension-type headache (TTH). In this study, the efficacy of local lidocain application on anxiety and depression, its curative effect in patients with chronic TTH have been investigated.

Methods: 48(24 lidocain,24 saline injection group) TTH patient had enrolled to our study. Injections were applied to the trigger points of the muscles innervated by C1-C3 and trigeminal nerve; exit points of the fifth cranial nerve; around the superior cervical ganglion. Three sessions were performed to patients at every three days. Patients were evaluated before, three months after treatment.

Results: In lidocain group, number of painful days in a month (PDM) had decreased from 20.2 to 7.5, visual analogue scale (VAS) values had decreased from 77.5 to 38.7, number of the analgeics used in a month (AUM) had decreased from 9.8 to 3.9, Hamilton depression score (HDS) had decreased from 20.0 to 14.8 and Hamilton anxiety score (HAS) had decreased from 21.9 to 14.6 after the treatment. In placebo group, number of PDM had decreased from 19.1 to 17.6, VAS values had decreased from 76.2 to 70.0, number of the AUM had decreased from 10.1 to 9.0, HDS had decreased from 20.2 to 19.2 and HAS had decreased from 21.7 to 20.3 after the treatment. All parameters have found to be improved in lidocain and placebo group (p< 0.05), response to lidocain group was better(p< 0.001).

Conclusion: Our findings suggest that local lidocain administration can be an effective method in the treatment of chronic TTH.

PS2-97
Adrenal insufficiency presenting as postural tachycardia syndrome
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Objectives: To report a case of adrenal insufficiency presenting as Postural Tachycardia Syndrome (POTS).terribleld

Background: POTS is a disorder of unknown etiology characterized by orthostatic intolerance and excessive tachycardia.
POTS is believed to be caused by central hypovolemia. Other causes of hypovolemia such as anemia, dehydration, hypothyroidism should be excluded before establishing diagnosis of POTS. Adrenal insufficiency has not been described before as an etiology for POTS.

Methods: Case report

Case report: We report a case of a 20 year-old woman who presented first to our institution for migraine headache. Headaches improved after hydration and treatment with nonsteroidal anti-inflammatory drugs, and was discharged home. She returned to emergency room 2 weeks after discharge, with dizziness and recurrent falls associated with loss of consciousness that occurred while she attempted to stand.

Physical examination showed orthostatic tachycardia with increase in heart rate from 70 to 130 with stable blood pressure.

Neurological exam was significant for gait instability. Tilt table test was positive. A diagnosis of POTS was made.

No major improvement was noticed with fluid hydration and treatment with fludrocortisone. Additional work up showed low morning cortisol level. A diagnosis of adrenal insufficiency was made and patient was placed on prednisone with relief of her symptoms.

Conclusion: POTS remains a diagnosis of exclusion. Here we report the first case of POTS associated with adrenal insufficiency, which was successfully treated with prednisone with relief of her symptoms.

PS2-98

Headache-related burden and willingness to pay for headache treatment in the republic of georgia

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Background: Using data from a recent population-based survey in the Republic of Georgia, we report on headache-attributed burden and health-related quality of life amongst people with headache and their willingness-to-pay for effective headache treatment.

Methods: Biologically unrelated adults from randomly-selected households in Tbilisi and Kakheti were interviewed using a structured diagnostic questionnaire, the MIDAS questionnaire and SF-36. The bidding-game method was employed to assess willingness to pay (WTP).

Results: Of 1,145 respondents, 50% had episodic headache (migraine or tension-type headache) and 7.6% had headache on ≥15 days/month which was not further diagnosed. MIDAS scores were higher in people with headache on ≥15 days/month than in those with episodic headache (P=0.004). People without headache had higher (better) scores in all SF-36 sub-scales than those with headache, but no differences were found between different headache types. A large majority (93%) of respondents with headache reported that they would pay an average of USD 8 per month for effective headache treatment. WTP did not correlate with headache type or frequency, or with MIDAS or SF-36 scores.

Conclusion: People in Georgia are heavily burdened by headache. Despite a general scepticism amongst those surveyed that headache could be recognised as a serious medical problem, even those less-affected indicated willingness to pay for effective treatment if it were available.

PS2-99

Cluster headache and smoking- what is the relationship?

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Cluster headache is a primary headache disorder which falls into the diagnostic category of autonomic cephalalgias along with trigeminal neuralgia in the IHS Classification - IHCD II(Cluster headache and other trigeminal autonomic cephalalgia). It is more commonly an episodic phenomenon but can also occur in a chronic form. Either form is rare with a prevalence of 0.2-0.4% and is more common in men than women. Although the pathogenesis of the condition is not well known it is characteristically associated with men in their middle age and smoking. Alcohol is a known dietary trigger factor but what is the
relation of smoking? It has always thought to be a contributory factor in cluster headache, but is the role more complicated than originally thought?

This report presents a case of a 53 year old gentleman who had a sporadic episode of a cluster headache several years ago. The patient smoked 10 cigarettes a day for the past 10 years. However since giving up smoking eight months ago he has suffered frequent episodic cluster headache attacks which wake him at night on a regular basis and have required the use of corticosteroids, high flow oxygen and prophylactic verapamil. He does not drink alcohol.

This report questions the role smoking plays in cluster headache and whether it played a protective role in this case, or whether giving up smoking triggered secondary physiological changes which may have more widespread implications in furthering our understanding of cluster headache aetiology.

PS2-100
Pathogenetic therapy of headache in ischemic cerebrovascular disease

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Background: Symptomatic atherothrombotic disease of extracranial arteries (internal carotid artery and vertebral artery) is frequently associated with headache different intensity and localization. The aim of investigation is study efficacy of dihydropyridine-derivative Ca(2+)-channel blocker-nimodipine in therapy of headache at patients with ischemic cerebrovascular disease.

Material and method: Twenty six patients at the age of 56-72 years with severe extracranial atherosclerotic disease, suffering from chronic daily headache were selected for this study. All patients had recurrent TIA or consequences of ischemic stroke. Quantitative evaluation of neurologic focal signs, neuropsycho-logical research and cognitive functions were assessed according Hachinsky scale and Mini Mental Stat Examination Scale. The dynamics of cerebrovascular blood circulation was investigated on duplex ultrasound imaging. In all cases electromyography of pericranial muscles for exclusion significant muscular tenderness in development of headache was used. Dynamics of pain was measured by visual analog scale. Course of treatment included nimodipin prescription daily dose 90mg for 45 days.

Results: By analysis the efficiency of nimodipin in 19 patients (70.3%) was shown. The positive effect was ascertain at reduction of headache up to 2 at 5 points according visual analog scale after course of therapy. In 20(74%) cases increase cognitive functions degree according with Mini Mental Stat Examination in 2-3 scores was observed. In 18(66.6%) cases positive hemodynamic effects of nimodipin as reduction of pulsality index(PI) and vascular resistance, improvement of cerebrovascular reactivity mainly in vertebrobasilar regional blood flow were observed.

Conclusion: Nimodipin provides significant decrease of headache intensity at patients with ischemic cerebrovascular disease.

PS2-101
Migraine associated with ovulation: clinical characteristics in japanese female migraineurs

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Objectives: To clarify the clinical characteristics of migraine associated with ovulation among Japanese women.

Background: The relationship between migraine and estrogen is well studied and MacGregor established the concept of menstrual migraine in 2004. Migraine is also provoked in ovulatory phase, but the mechanism is not revealed satisfactorily.

Methods: 67 female migraineurs who have regular menstrual cycle (15-54 years, mean age 38.8±8.4) treated at our headache clinic of Konan Hospital in 2007 (total menstrual cycle of 172) were evaluated retrospectively. We examined the frequency/severity of migraine attack and nausea/vomiting in ovulatory phase. We made a definition of “ovulatory day” (called Day1) as fifteen days before the first day of menstruation, “ovulatory phase” as from Day -2 to Day 3, and “peri-ovulatory phase” as each 3 consecutive days before/after ovulatory phase.

Results: Migraine attacks occurred in 224 days (26.0%) out of ovulatory phase and the number was reduced to 187 days (18.1%) in peri-ovulatory phase (p<0.0001). Mild migraine occurred more in ovulatory phase (0.122 attack/day) than in peri-ovulatory phase (0.076 attack/day) (p<0.001). However, there was no significance for moderate/severe migraine, nausea/vomiting in between ovulatory and peri-ovulatory phase. If we called the case migraine occurred in ovulatory phase 2 out of 3 menstrual cycles
and more, “ovulatorily-rerated migraine”, 39 patients out of 52 (75.0%) had ovulatorily-related migraine.

Conclusions: In Japanese female migraineurs who have regular menstrual cycle, migraine was significantly provoked more in ovulatory phase, similar to in menstrual phase. It is clinically important to recognize the ovulatorily-related migraine.

PS2-102
The role of personality in patients with chronic posttraumatic headache
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Introduction and aim: Patients with chronic posttraumatic headache (CPTH) after mild traumatic brain injuries may develop multiple symptoms. The relationship between a minor head trauma and the symptoms developed can seem non-equivalent. Thoughts of the role of patient’s personality and their coping strategy have been suggested in relation to the development of CPTH. The objective of this study is to describe the role of personality using a measure of “normal” personality.

Method: The Revised NEO Personality Inventory (NEO-PI-R) is a 240-item questionnaire for assessment of personality in accordance with the Five Factor Model. Each of the five factors; Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness, consists of six facets describing the factor in more detail. In The Danish Headache Centre there’s an ongoing large research project regarding the role of personality and treatment of CPTH and eligible patients are consecutively included. Data are compared to an age-gender matched reference material from the Danish population.

Results: 21 women and 8 men were included (mean age 35 years, range 18-63). The results indicate that CPTH patients score slightly higher on the factor Neuroticism, supported by the facets anxiety, angry hostility, depression and vulnerability. Extraversion is slightly lowered supported by the facet activity.

Discussion: These preliminary results suggest that clinical CPTH patients easily are distressed and overwhelmed by the pressure of their currently life situation. This indicates that psychological treatment should focus on stress management and self efficacy.

PS2-103
Toward a working definition of alcohol sensitivity
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Background and aims: There is no widely accepted quantitative definition of alcohol sensitivity in migraine. Variability exists, with authors relying on qualitative subject self-definition of their sensitivity to alcohol in general. This study investigates a working definition of alcohol sensitivity for migraine and other headaches, and characterizes differences between alcohol sensitive and other patients.

Methods: Our clinic collected 354 surveys on alcoholic and other dietary triggers of head pain. Our definitions were: alcohol sensitive is when ≤2 drinks of at least two types of alcohol always or often trigger head pain, and no alcohol type does not trigger with ≥4 drinks; alcohol insensitive is when at least two alcohol types are known to not trigger head-pain with <4 drinks, and no alcohol triggers with <4 drinks; and alcohol intermediate refers to patients who fit between these two definitions.

Results: Of 124 episodic migraine patients, 30.7% were sensitive, 52.8% intermediate and 21.9% insensitive. For chronic migraine (n=178) and NDPH (n=52), 25.3% and 17.3% were sensitive and 21.9% and 34.6% were insensitive respectively. As alcohol sensitivity increased, there was an increase in the number of years with headache, the percentage of females, the percentage with hangover headaches prior to development of their primary headaches, and the percentage with MSG sensitivity.

Conclusions: We have established a definition of alcohol sensitivity with both face and construct validity. Future studies of the clinical profile and pathophysiology of alcohol sensitivity may reasonably use this definition.

PS2-104
Fabry disease and headache
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Background and aims: Fabry disease is an X-linked glycosphingolipid storage disease resulting from a deficiency of lysosomal alpha-galactosidase. Ceramide trihexoside is accumulated in vascular endothelium and smooth-muscle
cells of various organs. The aims of the present study were to assess the following:

1) the headache profile in Fabry patients and
2) the effects of a treatment in Fabry patients with headache.

**Methods:** We have observed two brothers (aged 38 and 42 years) and their nephew (aged 26 years) who were known to be hemizygotes for Fabry disease.

**Results:** Both brothers and their nephew had been suffering from crises of non-pulsating headache since their youth. The headaches varied in duration, lasting from a few hours to several days. Episodic painful crises in the extremities and constant acroparasthesiae were present in all patients. One of the brothers and their nephew rarely developed episodes of pulsating headache with vomiting without aura. The meningeal signs were equivocal although the patients had non-infectious pleocytosis, intracranial hypertension and multiple old cerebral lacunar infarcts. Treatment with nonsteroidal anti-inflammatory drugs, carbamazepine and antidepressants was not effective. An attempt to treat the headache associated with aseptic meningeal reaction with prednisolone was successful.

**Conclusions:** Although the first brother has never experienced pulsating headaches with vomiting, we think that headache and aseptic meningeal reaction should be considered to be neurological complications of Fabry disease.

**PS2-105**

Celiac disease and migraine

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**Backgrounds and aims:** Celiac disease (CD) has been associated with neuropathy, ataxia and migraine. The aims of the study were to assess the prevalence of migraine in CD patients and the effects of a gluten free diet.

**Methods:** We have observed 376 patients with CD. The diagnosis of CD was confirmed endoscopically and by serum IgG antitransglutaminase and IgA antiendomysia. Control group consisted of 234 patients suffering from reflux-esophagitis. A gluten free diet was started in the patients diagnosed with CD associated with migraine, who were followed for 6 months.

**Results:** The average age was 32.56±6.3 years (range 15-48). Migraine occurred in 161 CD patients (43%) and in 25 control group patients (11%). Most CD patients had migraine attack once a month while the control group patients less than 1 attack a month. CD patients migraine attacks were less severe than the once in the control group. During the 6 months of gluten free diet, 112 of the 161 CD patients (2/3) had no migraine attacks, and the remaining 49 patients (1/3) experienced an improvement in frequency, duration, and intensity of migraine. Also we revealed the lack of compliance to gluten free diet in young CD patients with migraine.

**Conclusions:** An increased prevalence of migraine may be due to biochemical factors such as a lowered plasma serotonin, seen both in CD and in migraine, or an autoimmune mechanism. A gluten free diet may lead to an improvement in the migraine in these patients.

**PS2-106**

Primary headaches in patients with major psychiatric disorders

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The association of headache and psychiatric disorders such as depression and anxiety, is known for more than a century. The association of primary headaches and psychotic disorders is not investigated adequately.

The aim of this study was to estimate the frequency of primary headaches in patients with psychotic disorders.

The study was conducted in Special hospital for chronic major psychiatric disorders. The data about psychiatric diseases were collected from medical records and for headache from the interview and questionnaire designed for the study by neurologist (D.K.). Headache diagnosis was made according to ICHD-II criteria, and psychiatric diagnosis according to the ICD-10.

Seven-hundred and fifty patients were hospitalized for major psychiatric disorders during 2010 year. Only the patients with MMSE above 23 and without exacerbation of psychosis, 127 patients, were evaluable for the study. Twenty-three patients (18.1%) had headache. In headache group the most common was tension-type headache, 12 (52.2%) patients, followed by migraine without aura, 6 (26.1%) patients and migraine with aura 5 (21.7%). The attacks of headache were treated with triptans and non-specific analgesics, in addition to regular psychiatric treatment and treatment efficacy were obtained in 16 (69.6%).

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Patients with headache were older (50.3 ± 11.5 years) than non-headache patients (45.2 ± 9.7, p=0.03). There were no difference between groups according to gender and distribution of psychiatric diagnosis.

According to result of our study primary headaches are present in patients with major psychiatric disorders and should be treated. Further headache studies are necessary in these group of patients.

PS2-107
The effect of acetylsalicylic acid on patients with neck pain and tension-type headache - a pilot study
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Background: Neck pain causes considerable ill-health, and may contribute to tension-type headache (TTH). Acetylsalicylic acid (ASA) has a documented beneficial effect on TTH. However, it is not known how it influences neck pain. The aim was to assess the analgesic effect of ASA on neck pain in patients with neck pain and TTH.

Methods: Twenty-three subjects with frequent neck pain and TTH participated in two observation periods separated by at least one week, one treated and one untreated in random order; each lasting 5 days. In the treated period, subjects received ASA 1,000 mg 3-times daily for the first 3 days. In the untreated period they received no analgesics. Duration and intensity of neck pain and headache were recorded from 4 weeks before and during treatment periods, and additional measures of pain were recorded on day 3 of each observation period. The observer was blinded to treatment status.

Results: The 16 women and 4 men who completed the study had means of 25.7 days with neck pain and 20.4 days with TTH per month. Treatment with ASA reduced intensity x duration of neck pain by 26% compared with no treatment (P=0.01), while headache was reduced by 29% (P=0.06). Local tenderness of neck muscles was decreased from 12.2 to 5.0 mm on VAS (p=0.03) by ASA compared with no treatment.

Conclusion: ASA has an acute beneficial effect on neck pain and tenderness in the neck muscles. If this is confirmed under placebo-control, further studies should examine the potential for longer-term effects.
PS2-109

Health-related quality of life, disability and psychiatric comorbidity

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Headache frequency and duration provide incomplete information about the impact of headaches on quality of life. These factors influence prognosis and treatment. There are sparse reports comparing HRQL and psychiatric comorbidity in MOH- and non-MOH-patients. The study determines differences in headache-related disability, quality of life (HRQL) and the frequency of depression and anxiety between patients with (MOH) and without (nMOH) medication overuse headache.

Methods: Prospective study, 504 adult outpatients (mean age 42.3 years, female 90.9%) in a tertiary headache centre. ICDH-II-diagnoses: n=51 MOH and n=453 nMOH (57% migraine, 9.1% tension-type headache (tth), 33.9% migraine + tth). Headache scores included intensity and frequency of attacks, headache duration and medication. Psychiatric comorbidities, MIDAS, the SF12-inventory to investigate HRQL and the HADS using a PDA were recorded.

Results: MIDAS score in MOH was higher than in nMOH (mean 54.4/40.0;p<0.01). SF12-scales showed differences for physical well-being with lower scores for MOH (mean 36.9/40.2;p<0.05), but not for psychological scales (43.5/45.5;ns.). HADS-depression scores were higher in MOH (6.98/5.37;p<0.05). HADS anxiety scores were not elevated in MOH. No significant differences between groups were obtained for age, sex and duration of the disease. MOH had more headache days/month (15/7.6;p<0.001) and consumed more medication per month (14.9/4.4;p<0.001) compared to nMOH.

Conclusions: Our findings indicate a lower HRQL and daily functioning in MOH compared to other sufferers. In MOH depression scores were increased and physical well-being was decreased. We demonstrated that MOH patients report a high amount of headache-related disabilities shown by high MIDAS scores.

PS2-110

Iv ketamine: rapid treatment for all tac subtypes in the clinic

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Ketamine is an anesthetic agent that selectively blocks NMDA-type glutamate receptors at low doses. It has been shown to treat and reduce severity of a number of migraine and headache subtypes and implies glutamate as a pain promoting/ maintaining neurotransmitter system in the CNS.

We have shown effectiveness of ketamine in aborting refractory/chronic migraines, migraines with TN/facial pain and CDH in the clinic. We now present an extended/increased number of patients treated for TAC with the same medication.

15 patients with episodic/chronic cluster headaches, 7 with paroxysmal hemicrania[PH] and 5 with hemicrania continua [HC] were treated during flareups of their symptoms. Duration of symptoms was 5.9 years (range = 3-45 years).

After IV was started with monitoring, 0.3mg/kg of IV ketamine was infused over 2-3 hours. Headache severity [0-10 scale] was rated every 15 minutes by patient and staff. 14 patients were treated once/twice; the rest were treated up to 6 times.

Beginning severity of all TAC symptoms was 7.74/10; after treatment it averaged 2.2/10 with 8 patients reporting a 0/10 response. (p<.001). Duration of reduced headache severity (at least 50%) was 18.9 hours 9 (range 4-168 hours). "Spaciness" was reported in 12 patients and 3 had increased nausea. No dysphoric symptoms were reported.

IV ketamine can be given with safety and efficacy in the outpatient clinic for all TAC headaches. This complements prior effects of this medication and should be studied in double-blind studies, as glutamate may play a major role in the maintenance or causation of TAC.

PS2-111

Thunderclap headache as a manifestation of primary angiitis of the cns

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Background and aims: Thunderclap headaches (TCHs) are severe and hyperacute headaches with maximal intensity at onset, like a clap of thunder. TCH was recently discovered to be a presentation of many other diseases. We report a case of secondary TCH in a migraineur.

Case: A 53-year-old migraineur woman presented with severe headaches of abrupt onset, lasting a week.
She experienced an explosive and pulsatile headache in vertex area, which spread to her entire crania. She described her headache as being the worst of her life. There were nausea and vomiting. There were no autonomic symptoms and signs. She had been treated with non-steroidal anti-inflammatory drugs in a local hospital with suspected common migraine, but the headache was getting worse in severity. Initial physical and neurological examinations were normal. Her blood pressure was 168/88 mmHg and the pulse rate was 62 beats/min. Brain CT and cerebrospinal fluid tapping were normal. Brain MRI showed cortical subarachnoid hemorrhage in the right frontal area and mutifocal small infarctions. Conventional cerebral angiography revealed multiple arterial stenosis and dilatation involving both anterior and posterior circulation. Because of no known systemic vasculitis evidence, her diagnosis was probable primary angiitis of the CNS. With prednisolone and cyclophasphamide therapy for one month, her symptom and brain angiography was normalized.

**Conclusion:** This case demonstrates that a primary angiitis of the CNS can present with an isolated TCH. Clinicians should suspect the possibility of a primary angiitis of the CNS in patients with isolated TCH with migraine episodes.

**PS2-112**

**Prevalence of migraine and headache in moroccan schoolchildren**

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**Objective:** To determine the prevalence of migraine and headache in school children aged 6 to 13 years in the city of Agadir.

**Background:** This study is the first survey of headache in children in Morocco.

**Methods:** 1999 students were randomly selected using a multistage clustered sampling procedure. We used a questionnaire followed by an interview and clinical examination, between January and June 2004. 569 students who had reported having moderate or severe headache were interviewed and examined by a neurologist with the presence of their parents. Diagnosis of migraine headache was made according to the International Classification of Headache 2004.

**Results:** Participation rate was high (93.7%; 1874 of 1999).

From the questionnaire 52% reported a history of headache in the previous six months.

9% fulfilled the criteria for migraine without aura. Prevalence of migraine with aura was low (0.7%). Overall prevalence increased with age. The mean age of onset of migraine was 7.9 years. 52.6% had a frequency of occurrence of one to two attacks per month. In 58%, the headache lasted one to four hours. 64% had bilateral location. 79% had pulsating quality.

Prevalence of probable migraine was 1.2%. Prevalence of chronic migraine was low (0.1%).

84% had a family history of headache.

30% of children had missed school in the previous 3 months because of migraine attacks. 71% used over-the-counter drugs for migraine.

**Conclusions:** In school children in Agadir:

The prevalence of headache is high.

Migraine is a common health problem and is mostly underestimated and under-diagnosed.

**PS2-113**

**Medical treatments for short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (sUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (sUNA)**

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**Background:** Recent studies have reported some degree of efficacy of lamotrigine, topiramate, gabapentin and intravenous lidocaine in SUNCT. Few data are available on the treatment of SUNA.

**Aims:** To estimate the efficacy of abortive and preventive medications in SUNCT and SUNA.

**Methods:** A cohort of 62 SUNCT and 50 SUNA patients received open label treatments.

**Results:** Lidocaine 5% medicated patches were beneficial in 54.5% of patients (12/22). Intravenous lidocaine rendered 87% of patients (29/31) pain free, though the pain
tended to recur rapidly when treatment was stopped. A greater occipital nerve injection (GONI) was effective in 35.7% (20/56 patients), for a median of 14 days (range: 1-150 days).

Lamotrigine was effective in 67% of patients treated (59/88), topiramate in 44.4% (24/54 patients), gabapentin in 27.8% (17/61 patients) and carbamazepine in 45.6% (26/57 patients).

Oxcarbazepine was beneficial in 59% of patients (20/34), while the percentage of patients successfully treated with pregabalin was the same of those treated with gabapentin (12/43 patients); mexiletine was beneficial in 55.6% of patients (5/9), while duloxetine was beneficial in 38.5% (5/13 patients). No significant differences in treatment responses were noticed between SUNCT and SUNA.

Conclusion: Lidocaine is effective as short-term prevention, while GONI seems to be less effective in SUNCT than in cluster headache. Lamotrigine is the drug of choice. Oxcarbazepine and topiramate are recommended as second line treatments, while gabapentin and pregabalin can also be useful in some patients. Mexiletine and duloxetine might be new interesting options.

**PS2-114**

**Acute cephalalgia among women following endoscopic surgery**

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Endoscopic Foreheadplasty Surgery (EFS) is a minimally invasive surgical procedure performed to address undesirable facial aging or frown lines, correct genetic or traumatic facial deformities. The most frequent consumer of EFS are female, 91%, between the ages of 35-64. Case reports reveal EFS patients commonly report experiencing moderate to severe incapacitating postoperative migrainelike headache pain lasting 2-7 days. Undertreated pain continues to be a serious problem in the current health care system and is considered a health care priority. Approximately 50% of postoperative patients stated they were undertreated with pain medication 80% reportedly suffering for hours to days. EFS headache pain characteristics, medication management, impact on emotional and functional status, and associated factors have not been researched previously. Currently there is no explanation to the exact triggers responsible for postoperative craniotomy and migraine headache pains. EFS postoperative headache pain exploration is a human model potentially offering insight to understand EFS migraine-like headache pain experience and may offer new information on headache pain mechanisms for postoperative craniotomy and migraine individuals. This crucial first step to understanding headache pain for individuals undergoing EFS may lead to future studies to formulate effective strategies for those experiencing headache pain.

**Specific aims:** The purpose of this study is to examine:

1) headache pain characteristics;
2) current medications prescribed for headache pain and their effectiveness;
3) emotional and functional impact of headache pain; and
4) factors associated with headache pain.

**Methods:** 5 Private Surgical Offices. Migraine Questionnaire with Visual Analogue Scale.

**Results:** Pending.

**PS2-115**

**Description of migraine with persistent visual aura without infarction (pai) in a pediatric headache center**

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**Objective:** Describe the characteristics, evaluation, treatment, and outcome of children diagnosed with PAI.

**Background and aims:** PAI in children has rarely been described in the literature. The ICHD-II diagnostic criterion defines it as aura symptoms lasting for more than 1 week without radiographic evidence of infarction.

**Methods:** Retrospective analysis of 6,300 patients to identify and characterize those PAI meeting the ICHD-II criteria.

**Results:** PAI was identified in 8 patients (0.13%). Majority of patients were female (67.5%). Mean age at initial visit for girls were 12.6 years and boys were 10.3 years. Continuous aura was described in 8 patients including 1 patient who reported both a continuous visual and sensory aura. All patients had a normal neurological exam. Testing included brain MRI (62.5 %), brain MRI/MRA (37.5%), head CT (50%), EEG (62.5%) and vascular doppler studies (12.5%). MRI/MRA results-25% patients had
nonspecific frontal lobe signal abnormality. All EEG evaluations were normal. 75% of patients were evaluated by ophthalmology with a normal exam. Topiramate, levetiracetam, and divalproate ER were the most commonly prescribed medications. At last clinic visit of record, 37.5% of patients had resolution of PAI and 12.5% improved. Patients with complete PAI resolution were treated with topiramate or divalproate ER.

Conclusions: Incidence of PAI in children is uncommon yet can cause great concern to the headache provider, child, and family. Diagnostic testing can provide reassurance but does not offer understanding as to the pathophysiology. Children with PAI treated with topiramate or divalproate ER had the best outcomes.

**PS2-116**

Sudden headache after cervical epidural block: magnetic follow up for the pneumocephalus - case report

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Pneumocephalus can develop from accidental dural puncture using loss of resistance technique with air. Leakage of cerebrospinal fluid (CSF) or sudden headache following cervical epidural block may imply pneumocephalus.

A frequently used diagnostic tool of pneumocephalus is imaging such as computed tomography (CT). Herein, we report a case of pneumocephalus as a result of cervical epidural steroid injection under fluoroscopic guidance in a 46-year-old female patient with ossific cation of the posterior longitudinal ligament (OPLL).

We checked the brain MRI due to sudden onset of severe headache, and then detected the two air bubbles at both lateral ventricle.

7 days later, headache subsided and follow-up brain MRI showed pneumocephalus resolution.

**PS2-117**

Greater occipital nerve infiltration with cortivazol for cluster headache: a double blind randomized controlled trial

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Background: Greater occipital nerve infiltrations (GONI) are used for cluster headaches (CH). This trial studied the efficacy and safety of GONI with cortivazol (CVZ) in patients with CH having >2 attacks per day.

Methods: This randomized double-blind, placebo-controlled trial randomized 43 patients (15 chronic and 28 episodic) with active CH (>2 attacks per day) to GONI with CVZ or placebo (PL). Primary endpoint was the number of patients with a mean of ≤2 attacks daily following 3 GONI. Secondary endpoints included total number of attacks between Day 1 - 15, delay to remission and remission rate at Day 30, and frequency and severity of adverse events.

Findings: CVZ patients were significantly more likely to have ≥2 daily attacks following infiltrations than PL patients (95% for CVZ vs. 55% for PL; Cochran-Mantel-Haenszel-adjusted OR = 14.5; 95% CI = 1.79 to 116.87); they had fewer attacks over the first 15 days (mean difference = 19.7; 95% CI 6.8 to 32.6; p = 0.004) and had a higher remission rate at Day 30 (76% vs. 62%). CVZ patients went into remission a median of 7 days earlier compared to the PL patients (9 days (95% CI = 5.4 to 12.6 days) vs 16 days (95% CI = 4.0 to 28.0 days)). Adverse events did not differ between groups, and none was serious.

Interpretation: Repeated GONI with cortivazol can shorten a CH bout, decreasing the frequency of attacks and inducing a remission, both in episodic and chronic patients. It is safe and well-tolerated. This study was registered on clinicaltrials.org (NCT00804895).

**PS2-118**

Combined occipital nerve/supraorbital nerve stimulation for treatment of refractory headaches: initial adolescent experience (ages 12-17)

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Objectives: Assessment of the efficacy and safety of dual occipital-supraorbital nerve stimulation in adolescent headache patients.
Subjects and methods: Adolescents’ ages 12-17, including 10 females and 3 males were screened for implantation of occipital-supraorbital nerve stimulators. Each headache subject had failed standard therapies including dihydroergotamine 45.

Trial stimulators were placed across the occipital and supraorbital nerves. Criterion for a positive response was 75% improvement after a 3-5 day trial. Responders had an IPG (implantable pulse generator), which responds to an external programming computer, placed in the gluteal region.

Results: Eleven of 13 subjects had IPG implantation. Nine of 11 have continued to have good response. Two subjects initially had good response but later failed.

Sixty percent remain headache free. Twenty percent are still having some headaches but have had a 50% improvement. All were able to decrease their need for medication or stop medications entirely. All returned to school. Before implantation all were on a modified school program.

Conclusion: Combination occipital-supraorbital nerve neurostimulation provides an effective alternative treatment for adolescent patients with chronic severe headaches.

Conclusions: Headaches and functional movement disorders frequently occur in the same patient. Improved headache control can also result in improvement of the functional movements.

PS2-120
A better approach to evaluate the headache patient
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The last 20 years have seen a great improvement in our understanding of the headache patient among which was the systematic classification by the International Headache Society (IHS). Another important contribution was the epidemiological studies that added a new dimension of the problem. Without minimizing the psychological aspects, a new emphasis was put in the biological origin of migraine. But still, migraine headaches are considered to be under diagnosed under treated and responsible of tremendous disability.

In psychiatry, a major improvement happened with the introduction of the multiaxial approach to evaluation. The multiaxial system is not surprisingly, widely accepted. Many reasons account for its acceptance. It is a useful tool, comprehensive, and includes most of the factors that may influence the natural course of the disease and treatment. We propose a similar approach for the evaluation of the headache patient in the form of a multiaxial system that will encompass most of the comorbidities, complications, and important factors, sometimes forgotten or simply neglected.

THE MULTIAXIAL EVALUATION OF THE HEADACHE PATIENT

Axis I: type of Headaches as per IHS
a) Primary headaches
b) Secondary headaches
c) Cranial neuralgias, facial pain and other

Axis II: complications
a) Chronic Migraine
b) Mediation overuse

Axis III: associated conditions
a) Medical
b) Psychiatric

1) Clinical syndrome

2) Personality disorders and coping strategies

Axis IV: Psychosocial stressors

Axis V: Global functioning, disability impact (MIDAS)

We expect that with some adjustments or additions this multiaxial evaluation could better fulfill the needs of the headache physician.

**PS2-121**

**Migraine after the age of 50: clinical-psychological analysis**

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**Background:** The peculiarities of migraine (M) in the seniors are not well documented.

**Aim of the study** was to reveal clinical and psychological features of M in patients after the age of 50.

**Methods:** 30 pts aged 50 to 70 were examined using clinical interview, VAS, Leeds Dependence Questionnaire (LDQ), life quality (LQ) assessment (West Haven-Yale Multidimensional pain Inventory, WHYMPI), Beck Depression and State-Trait Anxiety Inventories. Based on disease course patients were divided into 2 groups: “persisting” (PM, n=11, m.age 52) and “regressing” M (RM, n=19, m.age 55).

**Results:** Retrospective analysis has shown that at the beginning pts with PM had more severe course both of M. At present PM group (vs RM) had the following significant (\(p<0.05\)) differences: less illness duration (37 and 43 ys), more frequent (3 and 0.75 per month), intensive (VAS 8 and 7) and prolonged M attacks (PM - 36 h, RM - 12 h), more frequent vomiting (72% and 10%) and postdrome (in 100% and 60%), used more dosed of painkillers (13 vs 5 tabs/month) and had more high dependence score (LDQ). Both groups had comparable levels of depression and anxiety, LQ decrease and high polymorbidity.

**Conclusion:** Although in most cases M is regressing with age in some patients it is persisting. Chief clinical factors determining persistence of M after the age of 50 are: severe course of M at the beginning and medication overuse/analgesic dependence. Further studies are required to elucidate pathophysiological mechanisms determining different migraine outcomes in the aged patients.

**PS2-122**

**Impact of organized headache care approach (one year experience in pakistan)**

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**Objective:** Awareness in primary care physicians, general public, community service & research.

**Material & methods:** Selected clinics/hospitals/medical centers where neurologists are not providing services to the community.

Prepare a week long awareness campaign by installing road side banners & distributing hand bills in the general public.

The material primarily focusing on the common sign & symptoms of the disease in Urdu.

People get registered where the activity going to be held.

**Change in Perspective:**

A- Physician’s:

Headache is a disease and not just some kind of psychological problem.

Headaches are to be treated by Neuro-physician’s.

Medication over dose can be prevented if patients are treated properly.

B- Patient’s:

Headaches are treatable.

Medication over use can result in drug induced headaches.

Migraine understanding improved.

Myths changed by realities.

Migraine can be managed and prevented by life style modification and proper prophylactic treatment.

**Results:**

A total of about 1345 plus patients were reported in 50 camps across Pakistan.
Number of patients with headaches: 987
Rest of 385 Patient’s were other neurological diseases.
Number of patients with Migraines: 567
Migraines most common between ages: 8yrs-43yrs.
Mostly self medications been used by the patients
90 % of patients were never told that they had migraines.
Only 5% of patients went to neurologist for consultation.

Conclusion:
We developed a model of organized headache care with the four components:
public awareness,
physician’s awareness
provision of free headache care
research.

This model could be implemented in other areas by professional and non-professional organizations.

PS2-123
Behavioural management of the triggers of recurrent headache: avoidance versus coping
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We have argued in three recent publications that the standard clinical advice that headache management should involve avoidance of triggers is open to criticism as it has minimal empirical support and problems with implementation. In addition, the literatures on anxiety, stress and chronic pain would suggest that avoidance is generally a maladaptive strategy. We have proposed the ‘Trigger Avoidance Model of Headaches’, which suggests that fear of the experience of headache drives susceptible individuals to try to avoid headache triggers, and this natural tendency is encouraged by clinicians and advice on the internet. Attempts to avoid triggers will result either in no exposure, or short exposure, to the triggers. This may lead to the capacity of the trigger to precipitate headaches being maintained or increased, through a process of sensitisation, failed habituation/adaptation, or lack of opportunity for learning to cope with the trigger.

The research described in this presentation is a randomised controlled trial that compares four approaches to behavioural management of headache triggers:
(i) Avoidance of all triggers (‘Avoidance’ - the traditional approach).
(ii) Learning to Cope with Triggers (‘LCT’ - uses approach/engage strategies whenever possible reserving avoidance for triggers where this is the preferred strategy).
(iii) ‘Avoidance + CBT’ (a control procedure that equates with the coping condition in terms of amount of treatment).
(iv) Waiting-list control (‘W-L’).

So far 41 participants have completed the pre- and post-treatment assessments. By the time of the Congress we expect to have analysed data on over 100 participants.

PS2-124
Underdiagnosis and undertreatment of migraine in spain. A study in migraine patients visiting the neurologist for the first time (primera study)
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Clinico-epidemiological characteristics of migraine patients attended for the first time in the neurology office were assessed in a Spain. A cross-sectional, multicenter study was carried out in which 168 neurologists recruited migraine patients. Sociodemographic, clinical, diagnostic and treatment characteristics of the patients were recorded. Disability was analyzed by using the Headache Impact Test (HIT-6) and the Sheehan Disability Inventory (SDI) scale. The study included 851 migraine patients, of which 74.6% were women with a mean age of 34.0 years (SD=10.7). Only 55.9% of the patients had a previous diagnosis of migraine. A considerable percentage of migraine patients are not adequately diagnosed, since 45% are referred to neurologists with the nonspecific diagnosis of ‘headache’. Migraine-associated disability was recorded with the HIT-6 Test. The disability of patients attended for the first time by a neurologist was found to be moderate or severe. Despite this, the use of specific treatment for migraine was low before visiting the neurologist (17.4%). After neurologist consultation, specific treatment for migraine (triptans) was recommended in a large percentage of cases (86.7%), and more than half of the patients (55.4%) received preventive treatment.

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whereas only 13.3% at first visit. In order to improve migraine management and treatment, it is necessary to secure a better diagnosis, established either by general practitioners or specialists. In our study, although the patients had important disability that should lead to the prescription of specific and preventive treatment for migraine, most of them were in fact taking non-specific medications and only a minority taking preventives.

PS2-125
Visual evoked potentials during withdrawal period in patients with medication overuse headache
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Background: Although the phenomenon of dyshabituation reflecting cortical excitability is documented in chronic migraine, similar studies in medication overuse headache (MOH) are not numerous.

Aim of the study was to evaluate cortical excitability in patients with MOH during withdrawal period (WP).

Methods: 16 pts with MOH (ICHD-2R), 9 with chronic daily headache without medication overuse (CDHwMOH) and 20 healthy controls were examined at baseline (before WP) and on 6-7 day of WP (CDHwMOH only at baseline) using checkerboard reversal-pattern visual evoked potentials (RP-VEP) with evaluation of grand average amplitude N75-P100 - result of all 500 averages, and habituation index (HI). It included reversal-pattern analysis of 5 five successive series of reversal-pattern visual stimulus; each series included 100 averages.

Results: Compared to controls both MOH and CDHwMOH groups had significantly (p < 0.05) elevated grand average N75-P100 amplitude (6.8, 7.12 and 7.48 μV); in MOH group before and on 6-7 day of WP (7.12 and 9.54 μV). In MOH group HI was markedly decreased before WP compared to on WP and controls (+2.7%, +4.8% and +12.5%); in CDHwMOH group HI was decreased vs controls (-11.2% and +12.5%).

Conclusion: The significant elevation in grand average N75-P100 amplitude could reflect cortical excitability increase during withdrawal period. Patients with MOH and with CDHwMOH are characterized by significant decrease in habituation index compared to controls. Maximum habituation decrease was seen in patients with CDHwMOH.

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PS2-126
Headache in patients of hospital for veterans of war with arterial hypertonia: specific features
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Research into the "high blood pressure headache" phenomenon began in 1913, when physician Theodore Janeway identified "morning headaches" as a common symptom of high blood pressure.

The science and physiology behind headaches support that increased blood pressure causes a phenomenon called autoregulation in the blood vessels leads to constriction of these vessels which is a very well known cause of headache symptoms. Tronvik E. et al (2008) had found that people with elevated, untreated high blood pressure were as much as 50% less likely to suffer a headache than were patients with similar health profiles but normal blood pressure. Nevertheless, the headache is still one of the most frequent complaints in patients with hypertension.

In our study, among the patients of Hospital for War Veterans with hypertension (mean age 54.2, all of them had received antihypertensive treatment) frequency of headache complaints was more than 90%.

In ¼ of the cases the headache tends to be pulsating in character, 1/3 it had tendency to unilateral localization. In half of the cases the pain is accompanied by nausea, more than in 80% of cases it increases during the movements. Main localizations of headache were frontotemporal and occipital regions. In ⅔ of cases patients suffer from chronic daily headache (more than 15 day in month); very often it also had some migraine-like features.

Among other complaints frequently declared were sleep disturbance (difficulty falling asleep - 84.6%), decreased memory and attention. Mean levels of anxiety and depression in HADS were within the normal range.

PS2-127
A study on efficacy of topiramate in the preventative treatment of migraine in females with high body mass index
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**Case report:** A 24 years woman suffered from FM since 2005. She felt exacerbation of widespread pain and headache with her position change; she felt severer widespread pain and headache in upright position than in lying position. So, she consulted our neurological outpatient clinic. We made a diagnosis of CSF leak with RI cisternography. We tried parenteral fluid therapy, but her symptoms continued. We noticed that she also suffered from POTS by the result of head up tilt test. We did epidural blood patch (EBP). After EBP, her widespread pain became easier and her headache diminished. After EBP, her clinical features did not meet with ACR criteria for FM.

**Discussion:** In this case, the parenteral fluid therapy was not effective. She had to take longtime bed rest because of severe headache. We suspected POTS complicated of FM. We consider that she suffered from FM, CSF leak, and POTS, because it is well-known that POTS tend to be complicated with headache. After EBP, her headache diminished and her widespread pain with FM became easier. This case shows CSF leak is one of the reasons of FM.

**PS2-128**

**Spontaneous csf leak complicated with fibromyalgia (case report)**

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**Background:** Patients with fibromyalgia (FM) and traumatic CSF leak are likely to suffer from severer signs and symptoms, such as increased widespread pain, than patients with fibromyalgia alone (Toda et al). It is also said that the patients suffering from FM tend to complicate postural tachycardia syndrome (POTS). We experienced a patient with spontaneous CSF leak complicated with FM and POTS.

**Objective:** To evaluate the efficacy of topiramate in the preventative treatment of migraine with high body mass index.

**Background:** Topiramate has demonstrated efficacy in migraine prevention in various studies so far. Migraine in India is widely prevalent in females. Certain anti migraine drugs are known for increasing body weight which is a social and physiological issue in females. We consequently conducted a placebo-controlled trial to evaluate the efficacy of topiramate for the preventative treatment of migraine in patients with high body mass index.

**Methods:** Forty two female patients, aged 14 to 50 years (mean, 28.2 years), were randomly assigned receive topiramate (n = 22) or placebo or other anti migraine drugs (n = 20; all women). Body mass Index (BMI) was calculated for all the patients. BMI more than 25 was considered to be overweight. Following a baseline phase of 4 weeks, the dose was titrated weekly in 25-mg increments over 8 weeks to the maximum tolerated dose followed by a 12-week maintenance phase. Reduction in migraine frequency and BMI were calculated at the end of the study period.

**Results:** During the study duration, 73% of the patients on topiramate and 36.36% of the patients on placebo achieved a more than 50% reduction in migraine frequency. Reduction in BMI occurred in 78.94% patients with topiramate when compared to 9.09% patients with placebo therapy. Only 1 of 20 topiramate-treated patients discontinued treatment due to memory impairment.

**Conclusions:** Preventative therapy with topiramate significantly reduced migraine frequency along with BMI in female patients.

**PS2-129**

**Headaches in the syndrome of the trephined**

B. Mokri

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The trepanation apparently common in ancient Peru has a long history. Nowadays decompressive craniectomies with creation of large cranial defects are performed often emergently as a life saving procedure in medically unmanageable cases of increased intracranial pressure of various causes often associated with increasing cerebral edema. In those who survive, sometimes a delayed post-craniectomy syndrome of neurologic symptoms, psychiatric changes and cognitive difficulties develop which often can be reversed with cranioplasty. Frequently encountered neurologic manifestations include headache, dizziness, tinnitus, unsteadiness, memory difficulties and spells of altered sensorium. Although headaches have been very common in this syndrome, there has been a paucity of description of the features of these headaches. A 37-year-old woman survived posttraumatic cerebral contusion and cerebral edema, having undergone a large frontoparietal decompressive cranioplasty. Good recovery took place in five months and her bone flap was placed back. Two years later there was gradual spontaneous resorption of bone flap, progressive sinking of the cranioplastic site along with the appearance of gait unsteadiness, speech difficulty, cognitive problems and bifrontal pressure-like non-throbbing and orthostatic headaches not aggravated by routine exertion and not associated with nausea, emesis, photophobia.

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sonophobia or osmophobia or allodynia. All symptoms reversed including complete resolution of the headaches following removal of the resorptive bone flap and reconstruction of bone defect and reconstruction of cranial defect with acrylic cranioplasty.

PS2-130
Preliminary results of an educational social network for patients and doctors against headache and cervical pain
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In previous studies we reported a significant reduction of headache and cervical pain using a cognitive and exercise program. We present here the preliminary data of an educational social network (www.noheadneckpain.com) for patients and doctors launched in November 2010.

Methods: After giving detailed information on characteristics of their headaches and/or cervical pain, applicants have access to demonstration videos and other material, constantly updated. Pain may be monitored with daily diaries and by the MIDAS after 3/6/12 months’ follow-up. In a reserved section clinicians have access to educational and scientific material.

Results: Up to February 1/2011, 991 patients enrolled (310 males, 681 females). Pain conditions were as follows: Migraine (M) = 112 (11.3%), Tension Type Headache (TTH) = 27 (2.7%), Myogenic Pain in the neck and shoulder area (MP) = 11 (1.1%), M+TTH= 30 (3%), M+TTH+MP= 194 (19.6%), M+MP= 458 (46.2%), TTH+MP= 159 (16%). Prevalence of M alone or in combination with TTH and/or MP was significantly (p < 0.02) higher in females (84.4%) than males (70.6 %). In both genders the superposition of MP significantly (p < 0.01) increased the prevalence and frequency of headache: chronic M with MP were 89 of 113 (78.8%), chronic TTH with MP were 49 of 51 (84.3%).

Conclusions: Neck and shoulder pain is an important and frequent comorbid disorder in patients with M and/or TTH and should be always evaluated and treated conjunctively. The social network can be an effective tool to analyze, monitor and prevent headache and cervical pain in extensive working communities and populations.

PS2-131
The treatment of resistant, chronic, headaches and facial pain patients in a comprehensive multidisciplinary clinic
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Background and aims: Medically unexplained symptoms including chronic non-remitting pain may comprise up to 25% of a tertiary neurological clinic population, causing severe disability to the patients, and a challenge to the physician facing patients who “tried already everything”. We hereby report our experience treating these patients with a multidisciplinary approach.

Methods: Resistant headache or facial pain was defined as non-remitting pain for at least 1 year; not attributed to another disorder; with a history of multiple consultations; failure of adequate treatments; accompanied with physical disability and impairment of working and social abilities. A multidisciplinary team establishes the treatment, consisting of drug treatment and at least 2 of the following: physical treatment (clinical massage, acupuncture or reflexology), hypnosis or biofeedback and psychotherapy (short or long term).

Results: Out of 1682 patients (66% women; average age 45 years) seen at the headache clinic during the last 18 months, 81 (4.8%) were referred to the multidisciplinary clinic (75% women; average age 50 years). Chronic tension type headache comprised 66% of the complaints, the rest being chronic migraine (21%), atypical facial pain (9%) and chronic cervical pain (4%). Changes were noted after 4-8 weeks of treatment, manifesting as improvement in the general well-being in 30% of the patients or reduction in the headache severity or frequency in 20% of the patients.

Conclusions: Multidisciplinary approach is helpful treating patients with non-remitting headache, considered previously ‘beyond help’. Enlarging treatment modalities may improve treatment outcome in these patients.

PS2-132
Detoxification is effective in patients with medication overuse headache. Introduction of the comoestas strategy
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Background: Depressive and anxiety disorders are associated with both migraine and vestibular disorders. Previous work has suggested that there is a specific association between migraine, vestibular disease, and anxiety disorders, but the precise mechanism is unknown. This study was designed to investigate the role vestibular symptoms play in the psychological symptoms associated with vestibular migraine.

Methods: Two groups of patients were studied. The first was a group of 39 patients with vestibular migraine according to Neuhauser's 2001 criteria. The second group comprised 44 patients with dizziness symptoms without migraine. Patients completed validated questionnaires (Beck Depression Inventory, Beck Anxiety Inventory, Vertigo Symptom Scale). Regression analysis was carried out to determine predictors of depressive and anxiety symptom scores.

Results: The migraine group had significantly higher scores on the anxiety (BAI median 19) (p=0.03) scales than the non-migraine group (BAI median 11). There was no difference in depression scores (BDI median 10 for migraine, 8 for non-migraine, p=0.57). The migraine group also scored more highly than the non-migraine group on the vertigo severity and frequency scales (VSS vertigo scale median 30 in the migraine group, 16 in the non-migraine group, p=0.003). Regression modelling showed that the high anxiety symptom scores were largely accounted for by the excess of vestibular symptoms.

Conclusions: This study has confirmed that patients with the vestibular subtype of migraine have high anxiety symptom levels when compared to non-migrainous dizzy controls, and suggests that this difference may be largely explained by high levels of vertigo symptoms.

PS2-134

Episodic headaches - looking beyond migraine

B.n. Krishna prasad

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Aim: To review the diagnosis of episodic headaches misdiagnosed as migraine, by primary care physicians as well as neurologists.

Methods: Detailed analysis of cases (n=7) of headaches diagnosed to have migraine. Elsewhere and treated accordingly. The methodology included thorough history with stress on frequency, severity, associated symptoms, precipitating/aggravating /relieving factors, diurnal variation etc. as well as re-looking at certain investigations and response to treatment,already received by the patients. The patients

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were subjected to other investigations wherever there was necessity viz; MRI/MRA,Ct angiogram,CSF analysis etc.

Results: There were 7 cases with M:F of 2:5 in age group of 32 to 69 years. All had headache which were episodic excepting one who had diffuse with episodic exacerbations of migraine like. The duration of headache varied from 1st time (7 days) to 30 years. I had cranial nerve symptoms (binocular diplopia) while 6 had no neurological deficits. 3 had subtle trigeminal autonomic symptoms. There was no papilledema in any. MRI/CT (head) was normal in 5. Subsequent MRI/MRA/MRV were abnormal in 4 while CT angiogram (intracranial, n-2) revealed abnormality in one. CSF studies carried out in 4 revealed no abnormality. The treatment in selected cases was individualised with variable degree of response. Excepting one there has been no long term follow up.

Conclusions: Migraine is the commonest primary headache disorder world over. The diagnosis is exclusively based on history. It can be often over diagnosed and hence mismanaged. One has to stress on the subtleties in the clinical features to get an accurate diagnosis and may need focussed investigations to diagnose the secondary ones mimicking migraine. This series with its various types of secondary headache is an eye opener in this direction.

PS2-135
Alterations of the cerebral venous circulation in children and adolescents with migraine assessed by transcranial doppler ultrasonography (TDU)
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TDU is a noninvasive tool to assess cerebral venous circulation. 42 patients with migraine aged from 6-15 years (19 girls and 9 boys) were enrolled into the study. 28 cases were classified as migraine without aura (MwoA) and 14 cases as migraine with aura (MwA). 28 subjects were examined as age-matched healthy controls.

The assessments were performed in the intermigrainous periods, in the horizontal body position, in active awakening after 15 minutes relaxation. TDU device was implemented with 2, 4, or 8-MHz range-gated transducers. Blood flow velocity was evaluated in the straight sinus (SS), ophthalmic and vertebral venous plexuses. Systolic linear velocity in the SS over 30 cm/s, presence of flow in the vertebral venous plexuses in horizontal position, flow reversal in the ophthalmic venous plexuses were considered as disturbances of the cerebral venous circulation, involving autoregulation mechanisms of cranial venous outflow. The disturbances were graded into mild, moderate and marked.

All patients suffering MwA had disturbances of cerebral venous circulation graded as marked in 85.8%, moderate in 7.1% and mild in 7.1%. Among the MwoA only 21.4% did not have any alterations, but 14.3% had marked, 25.0% moderate and 39.3% mild disturbances. The degree of cerebral venous circulation disturbances was found to increase with age: marked disturbances were revealed in 96% of migraine patients aged 10-16 years compared to 71% in aged 6-9 years. Thus, migraine pathogenesis may involve dysregulation of venous cerebral flow, which disturbances may progress with age and have impact on migraine attacks severity and frequency.

PS2-136
The role of overweight on headache, migraine and chronic pain in children and adolescents
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Background and aims: Migraine and headache features have been linked with overweight/obesity, specifically among women. Data among children/adolescence are sparse. We aimed to examine the association between obesity and various pain conditions in a population-based sample of children and adolescents aged 3-17 years.

Methods: Nationally representative health examination survey among 14,879 children and adolescents with standardized overweight measurement, comprehensive pain questionnaire and self-reported physician-diagnosed migraine. Overweight was defined as BMI >90th percentile.

Results: 3,406 had recurrent headache, 425 migraine, and 6,845 recurrent all-cause pain. The association between overweight and overall and specific pain conditions differed by gender and age. Among 3-13 years-old children, overweight was not associated with any pain condition, independent of gender. Among adolescence (14-17 year), we found significant associations of overweight with any of our pain outcomes for girls but not boys (p interactions all < 0.01). Girls who were overweight had age-adjusted increased odds ratio (95% confidence interval) of 1.57 (1.20-2.04) for all-cause pain, 1.70 (1.35-2.14) for recurrent headache, and 1.73 (1.17-2.56) for migraine.

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Adjustment for exercise made little difference. In further analyses of a smaller subsample with information on pain frequency, overweight was associated with pain chronicity (≥ several days/week), with OR from 1.33 (1.16-1.53) for all-cause pain to 2.61 (1.15-5.87) for migraine.

Conclusions: Results of this large, population-based sample of children and adolescence suggest that overweight not only relates to migraine but also to other pain conditions and that the association is limited to adolescence girls. We confirm associations between overweight and pain chronicity, which may start early in life.

PS2-137

Association between triptan use and cardiac contraindications in an insured migraine population


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Background and aims: Migraine is associated with cardiovascular diseases. The vasoconstrictive mechanism of triptans poses safety concerns for migraine patients with cardiovascular diseases and/or risk factors. This study assessed the association between triptan use and the presence of cardiac contraindications within an insured migraine population.

Methods: Ten representative health plans were randomly selected from the MedAssurant MORE2 Registry™. Approximately 2.5 million lives (ages 18-64) were covered during the measurement year (2009). Migraine patients were identified by a visit with a migraine diagnosis found in claim/encounter data, or if they had ≥ 2 episodes of headache seven or more days apart, or had at least one prescription for a migraine drug or migraine analgesic. Cardiac contraindications for triptans were defined as at least one prescription indicating a cardiac contraindication.

Results: 121,492 (4.9%) migraineurs were identified. Of the migraineurs in the sample, 38% had one or more prescriptions for a triptan and 24% had a cardiac contraindication. Thirty-seven percent of those with a cardiac contraindication had a triptan prescription during 2009 (38% of those 18-49 and 34% 50-64 years of age).

Conclusion: This study demonstrates potential concerns regarding pharmacotherapy for migraine. Over a third of migraine patients with cardiac contraindications had prescriptions for triptans filled in 2009, despite having cardiac contraindications. While we recognize that triptans remain the gold standard for acute migraine treatment, their high utilization (34%) among the 50-64 year old population with cardiac contraindications and who may be exposed to other risks, is concerning and deserves further study.

PS2-138

Headache at stroke onset in patients with basilar artery occlusion

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Background: Headache is frequent symptom in patients with cerebrovascular diseases and is more common in vertebrobasilar than in carotid territory strokes. Basilar artery occlusion (BAO) is an uncommon cause of stroke and the patients can present with various neurological deficits.

Methods: Among 154 consecutive patients with symptomatic vertebrobasilar territory ischemia, we identified 24 patients with BAO. The basilar artery occlusion and infarct locations were determined by magnetic resonance imaging and magnetic resonance angiography. Detailed information on clinical symptoms and signs, neurologic examination, stroke risk factors, and outcome was recorded in 15 patients with BAO in whom detailed information about the headache characteristics at onset could be obtained.

Results: Six patients (40%) with BAO, experienced headache at stroke onset. In the majority of patients the headache was mainly occipital or nuchal. The onset of the headache was sudden in third of the patients. The pain was described as dull in 50%, as pressing in 33%, and as stabbing in 27%. The mean duration of headache was 34 h. There was no association between headache at stroke onset and presumed etiology of the BAO. Intracranial stenosis or occlusion of vertebral arteries and stroke localization in the cerebellar hemisphere were associated with a higher probability of headache at stroke onset.

Conclusions: The headache at onset occurring among stroke patients due to BAO is frequent and primarily occipital in location. Lesion localization and stenosis of intracranial parts of vertebral artery were significantly associated with the probability of headache at stroke onset.
PS2-139

Internet based headache diary as an online diagnostic tool in headache center

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Background and aims: Filling in a diagnostic headache diary is helpful to identify the correct headache type and to describe accurately headache features and medications taken by patients. The aim of this pilot study was to test the usefulness and applicability of an Internet based diary in the diagnosis of primary headache disorders and medication overuse headache among patients treated in headache center.

Methods: This diagnostic diary is developed exclusively based on the ICHD-II criteria. The web application examines the diagnoses of migraine, tension-type, medication overuse and trigeminal autonomic cephalalgias on the basis of the variables needed to fulfill mandatory criteria. Twenty-four patients with Internet access agreed to fill the diary 4-6 weeks before their first consultation in headache center at the Institute of Neurology, Clinical Center of Serbia. We analyzed the patients’ level of compliance as well as the level of agreement between information gathered through clinical interview and the headache diary.

Results: Twenty out of twenty-four patients who participated in this study, fully completed the diary (83.3%). Their understanding of the diary proved highly satisfactory which was followed by good compliance. Patients, 75% of them, agreed that diary helped them to understand their headaches better. In 91.7% of cases, data obtained from the diary were sufficient for giving the correct diagnosis. The computer generated diagnosis and diagnosis given after clinical interview showed agreement in 21 patients.

Conclusions: Internet based headache diary can be considered as advanced, useful and reliable online diagnostic tool in everyday practice in headache center.

PS2-140

Psychiatric morbidity and headache, a thai study

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Background and aims: Despite the high prevalence and impact on health of psychiatric morbidity in patients with headache, to date there has been no systematic study of psychiatric morbidity of headache in Thailand. The aim of this cross sectional study was aimed to determine the prevalence of psychiatric disorders in patients with headache, especially migraine, at the Headache Clinic, Chulalongkorn Hospital, Thailand.

Methods: New Thai speaking patients to the clinic aged 18 and older were recruited. Demographic and disease-related variables were measured by a standardized questionnaire. Mental disorders, Risk for Mental disorder, and Type of Stress were determined by Patient Health Questionnaire (PHQ).

Results: Of the one hundred and sixteen samples were available to analyzed, the. The prevalence of depression, somatoform disorder, and anxiety disorder was found to be 27.4%, 30.1%, and 4.1% respectively. Headache type was not significantly associated with depression, somatoform, or anxiety disorder. Number of symptoms (OR=2.3, p<0.001) and stress related to health concerns (OR=3.8, p=0.007) significantly increased the risk for depression. Risk for mental disorder (OR=2.3, p=0.002) was significantly associated with an increased risk for somatoform disorder.

Conclusion: Although, a clear relationship between headache type and mental disorders was not evident, the results of this study will raise the awareness of physicians to be aware of the possible underlying mental disorders in patients with headache and facilitate appropriate treatment or psychiatric referral.

PS2-141

Indometacin-responsive headache syndromes in japanese

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Object: The aim of this study was to characterize indometacin-responsive headache syndromes (IRHS), which was not defined as a single category in the international classification of headache disorders, 2nd ed (ICDH-II).

Background: Chronic paroxysmal hemicrania (CPH) and hemicrania continua (HC) are unilateral headache highly responsive to indometacin, but they are classified into different categories in ICDH-II probably because of heterogeneous clinical features. CPH and HC are, however, suggested to be included in a single category of IRHS (Mathew 1981, Dodick 2004). IRHS represent a unique group of primary headache disorders characterized by a
prompt and often complete response to indometacin, and ineffectiveness to any other NSAIDs and medications.

**Methods:** We retrospectively analyzed clinical features in patients with IRHS examined at our hospital.

**Results:** Five patients were all women and their mean age was 54.6 years old (30-77). In all patients, headache was strictly unilateral, continuous nature with frequent paroxysmal exacerbation, and not responsive to NSAIDs other than their indometacin. Four patients accompanied cranial autonomic symptoms. None of them met the criteria for both CPH and HC exactly. Indometacin was started at 6 - 200 days after the onset with favorable result in all patients, including three who had a complete withdrawal of headache.

**Conclusion:** Our results support the suggestion of Mathew that CPH and HC should be included in IRHS.

**PS2-142**

**Vitamin d deficiency among pediatric patients with recurrent headaches**

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**Background:** Vitamin D deficiency is becoming increasingly recognized and has been associated with several chronic medical conditions. There have been studies that investigate a possible link between low vitamin D levels and chronic pain, however very few has been done in patient with chronic headaches and none within the pediatric population. Vitamin D deficiency, although reversible, is increasing in children and adolescents.

**Objective:** To determine the pattern of vitamin D deficiency in children and adolescents presenting to a tertiary pediatric headache facility with recurrent headaches including chronic daily headaches (CDH).

**Methods:** Vitamin D levels were obtained on patients with frequent episodic and chronic migraine for a period of one year. Serum 25-hydroxyvitamin D levels were obtained as part of standard of care.

**Results:** A total of 1148 vitamin D levels were drawn. Seventy percent of patients had 25-hydroxyvitamin D levels less than 30ng/ml, a level associated with vitamin D insufficiency while 30% of patients had 25-hydroxyvitamin D level less than 20ng/ml, a level associated with severe vitamin D deficiency. The lowest level occurred during the month of March and peaked in August.

**Conclusions:** Vitamin D levels are lower in patients with recurrent headaches compared to those among healthy pediatric population. There appears to be seasonal effect with low levels occurring during the late winter and peak levels during summer. The implications of low vitamin D levels in recurrent headaches are unknown. Further studies are needed to determine whether supplementation has the potential to improve headaches and improve overall outcomes.

**PS2-143**

**Evaluation of therapeutic efficacy in migraine patients in transitional stage of growth**

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**Background and purpose:** According to the clinical practice guideline for chronic headaches, ibuprofen and acetaminophen are effective acute-phase treatments for pediatric migraines. Since these medications target pediatric patients aged 6 - 12 years, we evaluated which medications would be most effective for migraine patients aged 3 - 13 years and < 15 years (transitional stage of growth).

**Results:** Subject 1 weighed 41 kg and the frequency of her headaches was high during menstruation. Migraine episodes occurred at dawn, and they were unilateral throbbing headaches on the left side accompanied by vomiting but without aura. The duration of episodes was 4±1.2 hours, and the frequency of episodes was 1 - 2 episodes a month. Her ADL was significantly suppressed during these episodes. For the first episode, ibuprofen and domperidone were administered orally. However, as no improvement was observed 2 hours after their administration, they were re-administered. For the 2nd episode, acetaminophen was administered in place of ibuprofen. However, the therapeutic efficacy of acetaminophen was only comparable with that of oral ibuprofen. For the 3rd episode, eletriptan 20 mg and domperidone were concurrently administered. A significant improvement in the headache was observed at 20 minutes post-dose, and subject’s satisfaction level was high.

**Conclusions:** We inferred that triptans can be considered as a 1st line therapy in migraine patients who are in
the transitional age of growth, show secondary sexual characteristics and weigh almost to the same as adults at 340 kg.

PS2-144

Are frequent and infrequent episodic tension type headaches different entities?

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Although none of the suggestive literature data, our clinical observations thought that frequent (FETTH) and infrequent episodic tension types headaches (IFETTH) could be different entities, except from their diagnostic criteria in ICHD-II.

In order to evaluate clinical differences of both of the disorders, we performed this multicenter, cross sectional, clinical-based study, including Turkish Headache Database Study group that accepted involving to this study.

Totally 1472 adult patients (807 FETTH and 665 IFETTH; mean age 45.8±15.5) selected from the database. Both of the disorders have same age, gender, attack duration characteristics. However, FETTH sufferers commonly described their headaches as pressing but IFETTH as blunt (p<0.001). Also headache location of patients with FETTH was generalized but of IFETTH in temples or unilateral (p<0.001). IFETTH attacks is more severe than others (p<0.001). IFETTH attacks generally onset in evening hours (p<0.001). Both of the comorbid systemic disorders, positive family history of medical disorders (headache, hypertension, diabetes mellitus, koronary artery disease, psychiatric disorders) and some associated symptoms (photophobia, phonophobia, sleep disorders, are commonly reported in patients with IFETTH. But associated diziness is more common in FETTH than IFETTH.

Our results suggested that two main subtypes of ETTH could be different entities far from their attack frequency and special survey of this differences could be lightened the basic mechanism of this disorders.

PS2-145

The effects of daily life variables on the frequency and properties of headache and its possible sociological reflections

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In this study we investigated the effects of in school and after school academic activities and performed hobbies on the frequency and properties of headache together with taking into consideration other social and medical variables.

The investigation universe was selected to be Icel Anatolian Lycee which accepts students with the highest scores in an examination performed province wide. As a result this would give us the chance of evaluating the condition of a group of students that represent the highest academic success in the province.

Totally 304 (49.7%) of the 611 students that were enrolled in the study were females and 307 (50.3%) were males. 87.2% of the female and 69.2% of the male students received a diagnosis of having headache (78.1% of the total, p=0.000). The majority had TTH (45.5%) followed by migraine (28.6%). Headache was more prominent in the 9th grade followed by the 12th grade and 10th grade students. The most frequently triggering component of their headaches were found out to be days of examinations (29.1%) and studying for extended hours (25.9%). Approximately 31.8% of the students were taking private lessons or attending courses. The lowest percent of happiness among the students (57.4%) and the ones who also spared the least time for their hobbies (2.97 h/week) was in the migraine group without aura (p=0.001).

This study put forward that headache is a frequently encountered problem in the young adults affecting negatively their academic and social lives and preventing their desires to participate in the social life.

PS2-146

Motivational interviewing as an approach to promote adherence and improve outcomes in adolescents with chronic daily headache

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Background: Few brief psychosocial interventions have demonstrated efficacy for addressing adolescent chronic daily headache (CDH). Motivational interviewing (MI) is a communication style that seeks to promote patient adherence by helping to resolve ambivalence about providers’ treatment recommendations. While MI has been
previously shown to address other issues (e.g., substance abuse), MI has not been tested as an approach to address adolescent CDH.

**Methods:** Forty seven adolescents (35 girls) ages 12-17 who met ICHD-2 criteria for medication overuse were randomly assigned to one of two conditions. The intervention condition \( (n = 23) \) involved a registered nurse providing up to four motivational interviewing telephone calls designed to promote adherence to a variety of a neurologist's recommendations (e.g., reducing over the counter analgesic use). The control condition \( (n = 24) \) involved a registered nurse telephoning solely to collect changes in contact information. 60 percent had chronic migraine, the remainder chronic tension type headaches.

**Results:** At baseline, the two groups did not differ on PedMIDAS scores, headache severity, or headache frequency. At the 4 month follow-up conducted by a blinded research assistant, the intervention group had lower severity scores relative to the control group (4.3 versus 6.0, \( p < .05 \)). There were nonsignificant encouraging trends indicating that the intervention group had lower PedMIDAS scores and headache frequency ratings relative to the control group.

**Conclusions:** MI is a promising strategy for improving outcomes in an adolescent CDH sample.

**PS2-147**

**Improvement in diagnosis and treatment in migraine and tension type headache with new meridian system**

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**Background:** Diagnosis and management of headache is based on a careful clinical approach. Many patients are put in the dilemma of underdiagnosis and undertreatment. Our knowledge of headache does not reach the goal to prove mechanism or pathophysiology definitely. IHS classification documents the pain location as one diagnostic criterion. The literature documenting location of primary headache is rare. There is no standard method to decide side and sites. We propose to use New Meridian and Acupuncture Points to determine the location.

**Subjects and methods:** This procedure was performed as one part of physical examination at department of neurology, Pusan National University Hospital from March 2009 to Feb. 2010. The 600 patients with primary headache without other neurological or systemic diseases were included. The patients were classified based on the international headache classification. We checked pain location on both sides of head and neck on New Modified Acupuncture Points on Gallbladder Meridian such and Urinary Bladder.

**Results:** There are several patterns of primary headache tension type headache and migraine headache. The numbers of pain location pattern were 15 kinds. We divided groups into pure migraine group, pure tension type headache group, and mixed form. The numbers of pure migraine pattern was 3, of pure tension type was 3, and of mixed form is 9.

**Conclusion:** Pain of primary headache is closely related with meridian systems esp. New Meridian System. We can improve the diagnostic and therapeutic value of migraine and tension type headache using new method, which is ease to practice.

**PS2-148**

**Psychiatric comorbidity and personality traits in patients affected by chronic daily headache**

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**Background:** Numerous studies confirmed the presence of mood and anxiety disorders in Chronic Daily Headache (CDH). Assessing personality traits with MMPI-2, CDH patients frequently show high scores in Hypochondriasis, Depression and Hysteria (defined as "neurotic triad"). It has been also suggested that anger may be involved in the chronification of migraine.

**Objective:** The aims are to: investigate the prevalence of psychiatric comorbidity and specific personality trait in CDH patients; investigate if specific personality traits characterize only patients with psychiatric comorbility, evaluate anger expressions levels.

**Methods:** M.I.N.I. (Mini International Neuropsychiatric Interview), MMPI-2 (Minnesota Multiphasic Personality Inventory) and STAXI (State Trait Anger Expression Inventory) were administrated to patients satisfying inclusion criteria for CDH. We recruited 94 subjects (72 women and 22 men). Patients were grouped according to the presence of psychiatric comorbidity (group A) or...
not (group B). Descriptive and comparative analyses were made.

Results: The 46.8% of the sample presented psychiatric comorbidity. Psychiatric disorders more frequent were mood (20.2%) and anxiety (17%) disorders. Only patients in group A presented the so-called "neurotic triad" in MMPI-2 scores. Group B showed high score only in Hypochondriasis. Both groups presented high scores in Health Concerns. In the whole group the higher score in STAXI was found in Anger/In subscale indicating a disposition to suppress rather than express anger feelings.

Conclusions: Only CDH patients with psychiatric comorbidity presented specific personality traits in our sample. Suppression of anger should be studied as possible risk factor for headache chronification.

PS2-149
Electrodermal responses to pain descriptors, neutral and emotional words among migraine sufferers and healthy controls
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Background and aims: Individuals with migraine may present a syndrome-specific descriptor profile and demonstrate greater skin conductance responsivity to migraine descriptors. Chronic pain patients have shown an increased reactivity to certain stimuli such as pain-related words, and emotionally-loaded words. The objective of this study is to analyse migraineurs reactivity to different stimuli and compare it to that of healthy controls.

Methods: 15 migraineurs and 15 nonmigraineurs observed a series of 10 pain descriptors, 10 neutral words and 10 emotional words. 30 trials were conducted in which participants’ skin conductance responses were recorded during the stimulus presentation. Participants were then asked to immediately recall the words, followed by an interference task, and a (delay) recall. All participants selected pain descriptors from the McGill Pain Questionnaire to describe migraines.

Results: Our hypothesis is that migraineurs will demonstrate greater skin conductance responsivity to the visual presentation of pain descriptors, confirming a syndrome-specific use of pain language. Migraineurs may be conditioned or sensitized to emotional words. Furthermore, it is expected that migraineurs will recall more pain words than healthy controls as individuals with chronic pain may present an enhanced attentional bias for pain-related words.

Conclusions: If confirmed, this would imply that migraineurs have a syndrome-specific descriptor profile. Interventions could be tailored at interfering with the learning process underlying the acquired additional meaning and significance of specific stimuli. Future research should emphasise the role of pain memories as peripheral responses to personally pain-related materials in individuals with pain may occur.

PS2-150
Chronic headache in children - therapeutic approaches
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Background and aims: Chronic headache is a rising therapeutic problem in all industrialized countries. Because of the unknown reasons for this phenomenon at lot of speculations and only very few studies have been done. Often unidimensional investigations did not show any convincing longstanding effects on headache items.

A change of paradigm could be observed during the last few years focussing on the functional aspects of children instead of the headache parameters.

Methods: 1100 Children suffering from chronic headaches for 3 years on the average were evaluated during the therapeutic process and one year after the intervention. A solution focussed brief treatment was started and continued once a month.

Results: A sample of 300 children an adolescents with an average age of 11 years gained an therapeutic effect of 73% which did not significantly changed over the following 5 years. Four hours of intervention was sufficient to reach this level. Quality of life improved as well as school attendance. Medication dropped to seldom intake rates.

Conclusions: The results show the effectiveness of an ambulatory intervention in chronic headache children and adolescents far away from spontaneous courses in a chronified pediatric population. The method is well evaluated by Steve de Shazer and Insoo Kim Berg from USA in psychic disturbances and could be utilized as well for outpatient headache therapy as shown in this investigation.
PS2-151
Cerebral toxoplasmosis may be a cause of recurrent headaches in children and adolescents

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Introduction: T. gondii (TG) infects about 30% of human population. It is believed that in immunocompetent hosts the infection is usually asymptomatic. Recently, Koseoglu et al. reported that in a group of 104 adult patients with migraine, 46 subjects were seropositive for anti-TG IgG antibodies.

Aim of the study: The purpose of the study was to establish frequency and characteristics of TG infection in the population of children hospitalized with symptoms and/or signs of the central nervous system abnormalities.

Methods: The study was performed in 93 children aged 1-17 years admitted consecutively to the Dpt of Pediatric Neurology from November 2009 to May 2010. Blood samples taken on admission were studied for the presence of specific anti-TG IgM, IgG antibodies and IgG avidity using enzyme immunoassay Platelia Toxo IgM, IgG.

Results: The study showed that 10 children (5 boys, 5 girls; 8-17 yrs old, mean age 14,2 yrs) had high anti-TG IgG antibody blood levels (range: 40,5-240 UI/ml, mean 142,19 UI/ml; positive value for IgG was ≥ 9 UI/ml). The avidity index (AI) ranged from 0,67 to 0,859 (scale: ≥ 0,5 high AI). Blood samples analyzed for specific anti-TG IgM were all negative. The headaches affected frontal (10 pts), occipital (4), and parietal areas (5), and usually appeared 1-2 times per month, lasted for 2-6 hrs, and had a mean intensity of 4.3 points in a 10-points subjective scale.

Conclusions: 10.7% of the studied children had specific anti-TG IgG antibodies, and high IgG avidity was characteristic for chronic infection.

PS2-152
Characteristics of migraine visual aura in southern brazil and northern usa

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Background: Migraine with aura (MwA) occurs in about 20% of migraineurs. Visual auras may manifest in many different ways.

Objective: To describe the characteristics of visual auras in patients with MwA.

Method: We have prospectively evaluated, from May/2009 to March/2010, 126 patients (103 women and 23 men) with the diagnosis of MwA, consecutively seen at the Clinica do Cerebro, Florianopolis, Brazil, and in the Ophthalmology Department of the University of Rochester, Rochester, NY, USA.

Results: 83.3% of the patients had the diagnosis of typical aura with migraine headache. 66.7% had exclusively visual auras. Typical aura without headache was reported by 4.8%. The mean age of the first migraine headache was 17.4±9.8 years; and the first visual aura 20.7±11.3. Aura started within the first year of headaches onset in 62.7%. 40.5% reported visual auras with all migraine headaches. Aura occurred exclusively prior to the headaches in 68.3%. The duration of the aura was 5-30 minutes in 65.1%. Aura symptoms originated in the peripheral visual field in 50.8%. Bilateral visual field involvement was described by 54%. Images moved across the visual field in 55.6%; and shimmered in 65.9%. Colorful auras were reported by 41.4% (20.7% had both colorful and black-and-white). The most frequent types of auras were blurred vision (53.2%) and small bright dots (46.8%); 40.5% described the classic zigzag lines. Most (74.6%) patients had just one aura pattern.

Conclusion: Migraine visual auras are heterogeneous and pleomorphic. Although they are classically described as in black-and-white, 41.4% of the patients reported colorful auras.

PS2-153
Hippocampal sclerosis and ipsilateral headache among mesial temporal lobe epilepsy patients

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Background: Migraine with aura (MwA) occurs in about 20% of migraineurs. Visual auras may manifest in many different ways.

Objective: To describe the characteristics of visual auras in patients with MwA.

Method: We have prospectively evaluated, from May/2009 to March/2010, 126 patients (103 women and 23 men) with the diagnosis of MwA, consecutively seen at the Clinica do Cerebro, Florianopolis, Brazil, and in the Ophthalmology Department of the University of Rochester, Rochester, NY, USA.

Results: 83.3% of the patients had the diagnosis of typical aura with migraine headache. 66.7% had exclusively visual auras. Typical aura without headache was reported by 4.8%. The mean age of the first migraine headache was 17.4±9.8 years; and the first visual aura 20.7±11.3. Aura started within the first year of headaches onset in 62.7%. 40.5% reported visual auras with all migraine headaches. Aura occurred exclusively prior to the headaches in 68.3%. The duration of the aura was 5-30 minutes in 65.1%. Aura symptoms originated in the peripheral visual field in 50.8%. Bilateral visual field involvement was described by 54%. Images moved across the visual field in 55.6%; and shimmered in 65.9%. Colorful auras were reported by 41.4% (20.7% had both colorful and black-and-white). The most frequent types of auras were blurred vision (53.2%) and small bright dots (46.8%); 40.5% described the classic zigzag lines. Most (74.6%) patients had just one aura pattern.

Conclusion: Migraine visual auras are heterogeneous and pleomorphic. Although they are classically described as in black-and-white, 41.4% of the patients reported colorful auras.
Background: Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) is a well-defined surgically remediable epileptic syndrome. Headache laterality may be useful to lateralizing the site of seizure onset.

Objective: To investigate the frequency and patterns of headache in a well-defined and homogeneous group of MTLE-HS patients.

Method: From May 2009 to April 2010, 100 consecutive MTLE-HS patients (55 females and 45 males), undergoing presurgical evaluation at the Centro de Epilepsia de Santa Catarina, Florianopolis, Brazil, due to refractory epilepsy, were prospectively evaluated. A structured questionnaire about their headaches was applied, using the ICHD-II diagnostic criteria for headache classification.

Results: Ninety-two patients (92%) had at least one headache episode during the previous 12 months. Migraine (all types) was diagnosed in 51.9% of patients and tension-type headache (TTH) in 39.1%. As expected, patients with migraine had higher frequency (p < 0.006), longer duration (p < 0.02), increased severity (p < 0.001) and lateralized pain (p < 0.002) than TTH ones. In comparison with ictal headache, peri-ictal headache was 3.9 times more likely to be associated with migraine than TTH (p = 0.01). MTLE-HS patients with unilateral hippocampal sclerosis (HS) and predominantly unilateral headache (irrespective of the type), significantly presented with the pain ipsilateral to the HS (OR 8.5; CI 95% 2.1-35.1; p=0.003).

Conclusions: Headache is a very common complaint in MTLE-HS patients. In patients with unilateral HS, there is a significant association between the predominant side of headache and the side of HS.

PS2-154

Headache among mesial temporal lobe epilepsy patients: a case-control study

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Background: Epilepsy and headache are two chronic disorders that are characterized by recurrent attacks. Subjects with epilepsy are 2.4 times more likely to have migraine than controls.

Objective: To investigate the 1-year prevalence of headache among refractory mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) patients compared with a non-epileptic control group.

Method: From May 2009 to April 2010, using a structured questionnaire, we investigated the prevalence of headache in a homogeneous group of 100 patients with MTLE-HS, undergoing presurgical evaluation at the Centro de Epilepsia de Santa Catarina, Florianopolis, Brazil, due to refractory epilepsy. The control group consisted of 100 age-matched subjects, from Santa Catarina state, in southern Brazil, who were randomized in a nationwide Brazilian Headache Study, which interviewed 3,848 subjects, from all 27 Brazilian states, between September 2006 and January 2007.

Results: There was a significantly higher prevalence of headache (92%) among the MTLE-HS patients when compared with the controls (73%; p = 0.001). Chronic daily headache (CDH) was significantly associated with MTLE-HS (OR 6.1, CI 95% 1.7 - 22; p = 0.005). We did not find any association between the diagnosis of migraine or tension-type headache and MTLE-HS.

Conclusions: This study showed that MTLE-HS increases the likelihood that the patient will suffer from headache. In addition, CDH was significantly more prevalent among the MTLE-HS patients than controls from the general population. In contrast to previous studies, we did not observe an association of MTLE-HS with migraine.

PS2-155

Iowa gambling task (igt) in medication overuse headache (moh) patients: a neuropsychological study of the orbitofrontal cortex functioning

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Background: Dependence behaviours are related to the orbitofrontal cortex (OFC) which exerts an inhibitory control on substance craving. The aim of this study was to explore the functioning of the OFC of MOH patients through neuropsychological assessment.
Method: We compared a group of episodic migraineurs without prior MOH and a group of MOH patients with IGT, a test aiming to detect decision making impairment as it is observed in patients with OFC damage and in drug addicts. In this test the subject is confronted with a decision that involves a conflict between an immediate reward and a long term negative consequence.

Results: Thirty five patients were included, 17 MOH and 18 migraineurs. The mean amount of acute headache medication taken per month was 82(+/−21.7) for the MOH group and 5.7(+/−1) for the migraine group (p=0.003). Mean MDH-Q score, a measure of dependence behaviour, was significantly higher in the MOH group than in the migraine group (85.2+/−5.8 versus 33.7+/−2.6 p=0.000), whereas mean catastrophizing score measured with PCS was not different between groups (28.3+/−3 versus 21+/−2.7) nor was mean BIS score, a measure of impulsivity (58+/−1.8 versus 57.5+/−2.3). Mean ITG score did not differentiate MOH patients from migraineurs, whereas it was significantly different between opiate abusers and other medication abusers (net score: 30.3+/−4.7 versus 4+/−8.4, p=0.04).

Conclusion: These results suggest a deficit of decision making processes underlying behavioural dependence in MOH patients who overuse medications containing psychoactive substances like opiates.

PS2-156
Prevalence of cranial autonomic symptoms in juvenile migraine: preliminary data
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Background and aims: Cranial Autonomic Symptoms (CAS) are frequently reported in adult migraineurs, but the prevalence of CAS in children affected by primary headaches is unknown. In addition, recent studies suggest a role of trigemino-autonomic reflex in the pathophysiology of pediatric migraine.

The aim of this study was to evaluate the prevalence of CAS in the course of headache attacks in a pediatric population with primary headaches and to study the correlation between CAS and the main symptoms of migraine.

Methods: A total of 74 children suffering from headache (M 34 F 40, aged 4-17 years) were enrolled from the 1th of September to the 31th of December 2010. A short supplementary questionnaire investigating the presence of CAS was administered to all children and their parents at the same time. The following CAS were included in our study: conjunctival injection, tearing, palpebral oedema, nasal congestion, rhinorrhhea, red ear, facial flushing, miosis, ptosis, forehead or facial sweating.

Results: Sixty-two children (83%) were affected by migraine, the remaining 12 (17%) by other primary headaches. CAS were present in 33 with migraine (53.2%) and only in 1 with episodic tension-type headache (8.3%). Two or more CAS were found in twenty-three (70%) children suffering from migraine during their attacks. The most common signs were red ear and conjunctival injection.

Conclusion: Although preliminary, these findings indicate that CAS are rather common in the course of pediatric migraine attacks. Besides, these results support the role of the trigemino-autonomic reflex in the pathophysiology of migraine.

PS2-157
Psychiatric comorbidity in patients with medication-overuse headache
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Background: Medication-overuse headache (MOH) is often associated with psychiatric disorders and they are known to be risk factors for chronicity and relapse after withdrawal therapy. There is emerging evidence on dependence and addiction in patients with medication-overuse headache.

Aim: The primary objective of this study was to investigate psychiatric comorbidities with a particular focus on dependence to headache medication in MOH patients as compared to a healthy control group.

Methods: Thirty-seven patients with MOH according to ICHD-II diagnostic criteria and 41 age-and gender matched healthy controls were investigated by a psychiatrist using clinical scales for depression (BDI, MADRS), anxiety (HAMA, STAI) and addiction (SDS, KFM), and a standardised interview based on DSM-IV diagnostic criteria (MINI).
Results: Twenty-six patients (70%) were diagnosed with depression according to the MADRS. Patients showed significantly higher anxiety scores than controls (median HAMA score 17; interquartile range (IQR) 19 vs. 2; IQR 2; p < 0.001). Thirty-four patients (92%) fulfilled DSM-IV criteria for substance abuse. Twenty-one patients (81%) fulfilled criteria for addiction disorder on the SDS and KFM scales. Prevalence of nicotine, alcohol, or illicit drug abuse was not increased compared to the control group.

Conclusion: In our sample, depression, anxiety, and substance dependence were associated with medication-overuse headache. Substance dependence might be an important disease maintaining factor in this patient group.

PS2-158
Enuresis in childhood migraine: a retrospective study
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Background and aims: PNE etiology is still unclear and described as multifactorial or/and biobehavioral, potentially involving neurological, urological, sleep, genetic, and psychological influences; moreover it could be considered as a comorbidity in many other diseases, such as obesity [1], sleep apnea [2]. The aim of our study was to assess the prevalence of bedwetting in childhood migraine without aura (MoA).

Methods: A retrospective investigation was performed on the clinical files of 223 children (114 females), mean age 8.94 ± 1.65 S.D. referred for MoA. PNE frequency was considered to be significant when it was ≥ 3 events/week. Results were compared with those from an age-matched control group (348 children, 197 females), mean age 8.76 ± 2.62 S.D., randomly selected from local schools in the Campania region.

Results: PNE prevalence was significantly higher in children with migraine 16.59% (33 subjects, 20 males) than in the control group 6.3% (22 subjects, 13 males) (Chi-square = 10.266; p = 0.001).

Conclusions: Our report is the first clinical study investigating the presence of PNE and MoA in a specific pediatric age range showing that a significant association might exist between these two conditions.

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References:

PS2-159
Separation anxiety disorders in childhood headache
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Background and aims: The close relationship between migraine and internalizing problems (i.e., anxiety) in childhood is well known. In developmental age the most frequent anxiety sign is the Separation Anxiety that could affect since the early age. Aim of study was to evaluate the prevalence of separation anxiety in a population of children affected by migraine without aura (MoA).

Methods: Study population was composed by 119 (69 M) MoA children (mean age 7.59 ± 1.78). Migraine diagnosis was performed according to IHS 2004 criteria. All subjects with previous psychiatric diagnosis, mental retardation, epilepsy, no migraine headache were excluded. All children and their parents filled out the Screen for Child Anxiety Related Disorders (SCARED) test. Among the SCARED subscales, only the separation anxiety (cut-off ≥ 5) was taken into account for our study. Results were compared with a 231 healthy subjects control group (114 M; mean age 7.64 ± 1.34). P value = 0.005 was considered significant.

Results: The prevalence of Separation Anxiety was more in MoA children than healthy control (6.83 ± 0.97 vs 4.72 ± 0.32; p < 0.001).

Conclusions: Our findings suggest the importance of an approach to migraine disease based on the care of the patient and his household, in order to allow a more accurate management of the psychological development of these patients.
PS2-160

Periodic syndromes in childhood migraine: a case-control study

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Background and aims: The International Headache Society (IHS) criteria of 2004 (4) computed only three “periodic syndromes” as precursors of migraine: Cyclical Vomiting Syndrome (CVS) [G43.82], Abdominal Migraine (AM) [G43.820], Benign Paroxysmal Vertigo of childhood (BPV) [G43.821].

In clinical practice, it’s well known that also other recurrent syndromes such as Growing Pains (GP), Periodic Fever (PF), Motion sickness (MS) and sleep disorders are very frequent in children with migraine, particularly in paediatric age range.

Aim of this study is to assess the role of periodic syndromes as risk factors for childhood migraine.

Methods: Study population consists of 441 subjects aged 6-13 years (mean 9.20; SD 2.42), consecutively referred for primary headaches, compared with a control group of 365 subjects aged 7-13 years (mean 9.08; SD 3.02), recruited in schools of Campania region.

Results: The two groups were matched for age (p = 0.539) and sex ratio (Chi-square = 0.002; p = 0.966).

Headache percentage distribution was the following: Migraine Without Aura (MoA) 38.32%, Migraine With Aura (MA) 11.11%, Episodic Tension Type Headache (ETTH) 16.78%, Chronic Tension Type Headache (CTTH) 30.63%.

The prevalence of periodic syndromes was less in healthy group respect of headache group (p = 0.003), and it was more in migraineurs than headache children (p = 0.0164).

MS is strongly associated with migraine (Chi-square = 46.217; p < 0.001), as GP (Chi-square = 6.010; p = 0.014).

CVS and AM shows no statistic differences in migraine group respect of headache subjects.

Conclusion: We suggest that MS could be included into IHS classification as childhood periodic syndromes.

PS2-161

Personality assessment of mothers of children affected by migraine

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Background and aims: The prevalence of migraine ranging between 2-5% in preschool age and 10% in prepubertal age, with a multifactorial etiology and many risk factors for exasperation of migraine symptomatology, in this point of view a key role is played by family.

Aim of our study is to assess the personality aspects of mothers of migraine without aura (MoA) children.

Methods: Mothers of 21 MoA children (11 M e 10 F; età media 8.4 ± 1.8) according to IHS-2 criteria, filled out MMPI-2 test.

Was considered only Basic (alfa di Cronbach = 0.91) and Content scales (alfa di Cronbach = 0.87).

Control group was composed by 48 mother of healthy children matched for age.

Results: Personality profiles of mothers of migraine children was different from mother of healthy children.

Specifically, Anx (p = 0.0079), Hea (p = 0.0217), Cyn (p = 0.0045), Lse (p = 0.0029), Wrk (p = 0.0096) scales.

Moreover, some scales show significant correlation with frequency (Anx r = 0.371, p = 0.002; Lse r = 0.441, p = 0.000; Wrk r = 0.315, p = 0.008) and intensity (Anx r = 0.404, p = 0.001; Lse r = 0.433, p = 0.000; Wrk r = 0.406, p = 0.001) of migraine attacks.

Conclusions: Our findings show the presence in mothers of migraine children of anxious behaviour, particularly in health concerns. The correlation between frequency and intensity of pain suggest the importance of mother personality in pain disperception of children with migraine.

PS2-162

Post-craniotomy headache: a cohort study

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Background: The incidence of Post-craniotomy headache (PCH) is highly variable (0-90%). Most studies are
retrospective. The aim of this study was to evaluate the risk of headache after craniotomy.

**Methods:** From May 2009 to October 2010, patients hospitalized in Hospital da Restauração, Brazil, for treatment of intracranial aneurysms were interviewed before the treatment through a semi-structured questionnaire and followed for up to 4 months. International Headache Society criteria for PCH were used for the patients with surgery and were adapted for headache after embolization (maximal intensity of pain in the same side of the aneurysm).

**Results:** Of the 101 patients included, 53 underwent craniotomy and 48, embolization. The surgery group had fewer women (60.4% vs. 79.2%, \( p = 0.04 \)) and was younger (mean 46.7 vs. 51.7 years-old, \( p = 0.05 \)). The incidence of headache after the procedure was 63% in the craniotomy group and 40% in the control group. The risk of headache was significantly higher after craniotomy (relative risk 1.55, 95% CI 1.03-2.33). In multivariate analysis, the risk of headache after treatment was higher in patients undergoing craniotomy (odds ratio 3.87, 95% CI 1.04-14.4) and in those with migraine diagnosis in pre-operative period (OR 4.60, 95% CI 1.11-19.0). The groups did not differ in the incidence of persistent headache after three months.

**Conclusions:** There was an increased risk of headache after treatment of intracranial aneurysms in patients undergoing craniotomy and in those who had migraine before treatment.

**PS2-163**

*Is onabotulinumtoxina a cost-effective therapy for chronic migraine?*

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**Background and aims:** Chronic migraine (CM), a primary headache disorder afflicting \( \sim 2\% \) of the general population, accounts for a disproportionate share of the direct and indirect costs associated with migraine generally. OnabotulinumtoxinA (onabotA) injection therapy has been shown to be effective in suppressing CM, but the cost of treatment is high relative to other therapies commonly utilized for migraine prophylaxis. We sought to determine whether the cost of treatment with onabotA may be offset by a consequent reduction in direct medical costs attributable to CM.

**Methods:** Using the PREEMPT dosing/injection paradigm, we administered open-label onabotA to 200 patients with CM who presented to a university-based headache center. Along with the patients’ clinical responses, we assessed the costs associated with emergency department (ED) utilization for acute headache over the 6 months preceding and following initiation of onabotA therapy.

**Results:** The gross charges associated with onabotA therapy totaled $702,120(US). Over the 6 months following initiation of treatment, the reduction in gross charges attributable to ED utilization totaled $806,257(US).

**Conclusion:** These data suggest that the reduction in direct medical costs related only to ED utilization that occurs consequent to onabotA therapy may be sufficient to offset the cost of that therapy.

**PS2-164**

*Onset of cluster headache after cataract surgery*

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**Objective:** To describe a case of new onset cluster headache subsequent to ophthalmologic surgery.

**Background:** There are several case reports of new onset cluster headaches after eye trauma, infections, orbital tumors or myositis, but only rarely after cataract surgery.

**Methods:** Case report and review of literature.

**Results:** A 61-year-old woman presented with a 15-month history of left-sided severe periorbital and temporal pain starting two weeks after an uneventful cataract surgery. The attacks occurred twice a day, in the early afternoon and evening with sharp, stabbing pain lasting 60 minutes associated with left sided conjunctival injection and lacrimation. Neurological and ophthalmologic examination was unremarkable. Neuroimaging including MRI of brain and MR angiogram of the head and neck did not reveal any structural etiology. She responded to Topiramate for preventive treatment, and Sumatriptan for abortive therapy.

**Conclusion:** An unusual case is described in which cluster headaches began immediately after cataract surgery and intraocular lens implantation. Literature review showed only one similar case where cluster headaches began immediately after cataract surgery. We hypothesize that intraorbital manipulation and implantation of a foreign
body activated the ophthalmic division of the trigeminal nerve, provoked pain in the periorbital region with subsequent activation of adjacent parasympathetic fibers. Although rare, our case presents a unique situation for further exploration of the underlying pathogenesis of cluster headache.

PS2-165
Factors associated with presence of tender trigger points on shoulder girdle muscles in occipital neuralgia
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Background: Presence of tender trigger points on the trapezius and rhomboids has not been previously reported in Occipital Neuralgia (ON). These trigger points are 4 of the 18 triggers that comprise the criteria for diagnosis of fibromyalgia.

Objective: To describe the frequency and predictors of trigger point tenderness in patients with ON.

Methods: We did a retrospective chart analysis of subjects with ON for presence of trigger point injections (TPI). Demographic data was collected including age, gender and ethnicity. The relationship between age, sex, race, migraine, trigger points and laterality was analyzed.

Results: 94 consecutive patients with ON (57% female, mean age 54 years) were included. The majority of patients were caucasian (51%) or hispanic (36%). Forty-four patients had a history of migraine, but none had fibromyalgia. Forty-four (47%) patients had at least one tender trigger point, of which 31 received TPI. Twenty-three patients had TPI on Trapezius, and 18 had trigger points on rhomboids. There was an association for congruent bilaterality of Occipital nerve block (ONB) with TPI. Of the 61 patients who received bilateral ONB, 13 had bilateral trapezius TPI (21%, p=0.061) and 11 received bilateral rhomboid TPI (18%, p=0.011). There was no correlation between age, gender, race, history of migraine headaches and presence of trigger points.

Conclusion: Patients with ON should also be screened for trigger points on trapezius and rhomboids even in the absence of fibromyalgia. Bilateral ON may have a higher frequency of bilateral trigger points.

PS2-166
Socio-demographic and occupational factors associated of migraine and tension-type headaches
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Tension-type headache and migraine headache comprise two thirds of various kinds of headaches. Correct diagnosis is the first and the most cardinal step for headache treatments. This study was conducted to estimate the prevalence of migraine and tension-type headaches (TTH) and to report of sociodemographic and occupational risk factors of migraine and tension-type headaches among hospital staffs of Shiraz (Iran). This was a case-control study using prevalence data a random sample (stratified random sample) of 1023 hospital staffs of Shiraz (Iran).

The subjects were 115(11.2%) patients with migraine and 199(19.5%) patients with tension type headaches diagnosed by IHS criteria. Of 115 patient with migraine were 97 (84.3%) female and 18 (15.7%) male, and of 199 patient with tension type headache were 154(77.4%) female and 45(22.6%) male. The most prevalence of migraine and tension type headache was among 30-39(16.5%) and 40-49 (25.8%) age group. TTH and migraine headaches were significantly associated with positive family history of headache, self reported abnormal sleep pattern and female gender (P < 0.001). Also TTH was negatively associated with total 24hr duration of sleep and positively associated with history of involvement in second job and systolic blood pressure. Treatment of sleep disorders can be an important factor in prevention of headache. Young women employees as a high-risk group requires special attention.

PS2-167
Clinical and epidemiological characteristics of migraine and tension-type headaches among hospitals staffs of Iran
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The headache is the most common pain syndrome. This study was conducted to estimate the prevalence of migraine and tension-type headaches (TTH) and to report on clinical characteristics of migraine and TTH with using the International Headache Society (IHS) diagnosis criteria. A random sample of 1023 staffs constituting a 20% sample of the hospitals staff population was selected. Sampling method was categorical random sampling. Within each group sampling was carried out systematically. Data were collected by screening questionnaire followed by clinical interviews, general physical and neurological examination, and diagnostic criteria of IHS. Prevalence of migraine, TTH and coexisting migraine and TTH were estimated as 11.2% (115 cases), 19.5% (199 subjects) and 3.2% (33 subjects) respectively. Clinical characteristics of headache including type, site, number, intensity, concomitant symptoms of headache had been surveyed. The average of prevalence of migraine and TTH were lower than their counter parts in western countries but higher than previous studies conducted in other Asian countries. Clinical characteristics were almost parallel with IHS criteria, missed work rates were higher for subjects with migraine headache, and also TTH and migraine were separate disorders and were not as a part of a continuum of headache disorders. Headache disorders deserve more attention, especially concerning strategies leading to adequate primary prevention, diagnosis and treatment.

Results: 45.6% of staff had poor mental health, prevalence among male and female were 27.6 (16 cases) and 54.3 (380 cases), respectively. Their average score in physical health, anxiety, social functions, depression and general mental health status were 6.72, 6.67, 6.48, 3.28 and 23.2% respectively. Results show that headache has a profound effect on mental health status and these two are not independent of each other. Mental health status had a meaningful relationship with steep pattern, physical activity and job satisfaction. Females had more odds to disorder.

Conclusion: Findings indicate that mental health disorders have a high prevalence; thereby authorities and researchers need to pay more attention to this issue, through identifying influential factors and developing intervention programs to improve the situation. High comorbidity between headache and GHQ requires specific strategy and intervention development. To improve the sleep pattern and make facilities available for physical activities, are essential for staff satisfaction.

PS2-168
Comorbidity between migraine and tension type headache with their mental health status

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The negative impacts of comorbidity of mental disorders and headaches has been well documented. This study was conducted aiming in assessing the mental health status of human resources of Shiraz hospitals, occupational risk factors and relationship between migraine - Tension Type Headache and their mental health status. The sample size includes 1023 Shiraz hospital staff. The subjects were selected using categorical random sampling method. Data was collected using a questionnaire, which included demographic, occupational status. The health status was assessed using GHQ 28 standards. The diagnostic criteria of type of headache were done by using international headache society standards.

Results: The informants mentioned to a variety of herbal plants and home procedures. A mix of egg yolk, and powder of raw peas or mix egg yolk, yogurt and cedar or cedar, egg yolk, henna, Fumaria parviflora and water were used as dressing on the head. Tie firmly the head with a headband, needling between eyebrows to bleed and putting ash and needling on temporal area and doing some traditional rituals to make away devil eye, are the other home procedures to relief pain.
Conclusions: Health care providers should be aware of these remedies, to educate people about remedies that may be harmful. Most remedies used pose no threat to health. In some cases, remedies may be blended with traditional medical treatments to ensure better patient compliance.

PS2-170

The large-scale epidemiological study of the chronic headache among health care and welfare professionals in Japan

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Objective: We conducted an epidemiological study to clarify the status of chronic headache among health care and welfare professionals.

Methods: The subjects were 1,735 employees working in affiliated hospitals and nursing facilities. In September 2010, we conducted a questionnaire survey to ask questions regarding chronic headache.

Results:
1) We collected 1,281 valid responses, 37% of which (21% for males, 42% for females) reported chronic headache.
2) The prevalence was highest among the subjects in their thirties for both males and females (25% for males, 49% for females).
3) The prevalence was highest among caregivers (41%), followed by nurses (39%), clerical staff (32%), laboratory and other technicians (31%), rehabilitation staff (29%), and physicians/pharmacists (19%).
4) While 29% (14% for males, 34% for females) of the subjects had migraine, 6% (8% for males, 6% for females) experienced tension headache.
5) Although the consultation rate was as low as 26%, 58% of the subjects were administered drugs.
6) A large percentage of the subjects (62%: 31% for tension headache, 66% for migraine) reported negative effects on their work.
7) Whereas 12% left early or were absent from work due to headache during the past year, 11% reported that their careless mistakes that could lead to a major accident were caused by headache.

Conclusions: This large-scale survey involved more than 1,000 subjects, and the results will hopefully serve as exemplary data on chronic headache involving health care and welfare professionals in Japan.

PS2-171

Are there predictive factors of migraine outcome after menopause?

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Introduction: Changes in hormonal levels can induce significant headache modifications. At menopause migraine can regress, worsen or unchange: the possible factors associated with the different outcome are unidentified yet.

Aim of the study: To define some of the predictive factors of migraine outcome after menopause.

Materials and methods: We considered 291 post-menopausal women suffering from migraine according to ICHD-II criteria, observing if and how the characteristics of migraine changed after menopause, and possible predictive factors of the outcome, like menses/migraine association, number of pregnancies, use of estroprogestinic pills and outcome in their mothers if there was a positive family history.

Results: In 48 (16.5%) of the patients migraine improved after menopause, in 243 (83.5%) worsened or didn’t change.
44 (91.7%) of the improved patients had period-related migraine attacks, vs only 174 (71.6%) of the worsened patients (p< 0.05). 7.1% of the improved patients had more than two pregnancies, while 18.6% of the unchanged/worsened women bore more than two children, suggesting that a higher number of pregnancies can predict a worse outcome (p = 0,034).

The worsening of migraine after menopause followed the patients’ mothers outcome in many cases with positive family history (p = 0.04).

Discussion: The association of migraine attacks with periods and the improvement of migraine after menopause in the patients’ mother seem to predict a post-menopausal headache improvement. More than two pregnancies could affect negatively symptoms after menopause.

More studies are needed to confirm these data, in order to predict a prognosis and tailor therapies to each patient.

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Successful treatment of headache in five adolescence by sonography-guided injection of botulinum toxin type a into myofascial trigger points

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Headache is the most common reason for children and adolescents to request medical help. Most pathophysiological concepts of headache mention the role of focal muscular hypertension as to trigger or to sustain the pain. Treatment strategies have produced controversial results up to now, but botulinum toxin was approved for the treatment of adult migraine in Great Britain in 2010. We report the successful analgesic treatment of five adolescents using sonography-guided injections of botulinum toxin type A (BoNT/A) into myofascial trigger points (mfTP).

Within a two-year period 180 patients were evaluated at our headache clinic. Among those five patients

(i) suffered from chronic headache for at least 6 months (mean duration 1.9 yrs.),
(ii) had mfTP in cervical and/or shoulder muscles, and
(iii) treatment failed with analgesics and physical therapy incl. relaxation techniques.

Four weeks prior to treatment the mean headache frequency was 27 days per month, mean severity was 6.6 (range 6-8/10) on a visual analogue scale (VAS). The five patients underwent sonography-guided BoNT/A injections in one or two mfTP (10-25 U Botox®) per site. Four weeks after treatment, all patients reported a decrease in headache frequency (mean 4.8 days per month) and headache severity (VAS mean: 2.4, range 0-5). Following successful treatment the adolescence regained the ability to fully participate in schooling and social activities. A follow up questionnaires will focus on these topics in more detail.

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Reliability and validity of the acute medication self-efficacy scale for headache

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Little research has examined factors associated with taking acute medication optimally. Social Cognitive Theory suggests that acute medication self-efficacy, confidence in one’s ability use acute medications optimally, is essential to routinely engage in these behaviors. This study aimed to develop and provide initial psychometric information for the Acute Medication Self-Efficacy Scale for Headache (AMSE-H).

Interviews with headache sufferers (n = 21) and health care providers (n = 15), and item selection using data from an additional 35 headache sufferers resulted in the 6 AMSE-H items. An additional 161 additional migraine sufferers completed the AMSE-H and single-item measures of overall acute medication self-efficacy, acute medication outcome expectancies, and perceived access to acute headache medication. 58 of these participants, who previously received behavioral treatment, also completed the Headache Management Self-Efficacy scale, a measure of confidence in one’s ability to manage migraines using behavioral techniques.

The AMSE-H demonstrated adequate internal consistency, α = .76, and one-week rest-retest reliability, r = .72, p < .001. Higher scores on the AMSE-H were associated with overall acute medication self-efficacy (r = .73, p < .001) and theoretically relevant constructs, including expectations that acute medication can reduce headache severity (r = .26, p < .01) and headache frequency (r = .21, p < .01), perceived access to acute medication (r = .29, p < .001), and the Headache Management Self-Efficacy scale (r = .29, p < .05).

Preliminary evidence suggests that the AMSE-H is a reliable and valid instrument to measure acute headache medication self-efficacy.

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Headache and blurred vision presenting signs of hypophysial plasmacutoma

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Case report: A 37 -year-old woman with 2-month history of headache and blurred vision was referred for work up. She had diplopia from one week ago. She had no positive finding in past medical history, her systemic examination was normal, routine lab study unless skull x-ray was in normal limit. In neuroexam she was alert and
awake, bilateral six nerve palsy, bilateral pupilledema, normal motor, sensory and cerebellar exam were recorded. No noccal rigidity was detected.

Memory and judgement were normal. She was found to have an intrasellar mass simulating a large and invasive pituitary adenoma. Further studies confirmed the diagnosis of multiple myeloma. The patient was successfully treated with surgery, radiotherapy followed by systemic chemotherapy. Because they have different therapeutic implications, extramedullary plasmacytomas involving pituitary gland should be considered in the differential diagnosis of a non-functioning pituitary mass.

Conclusion: Plasmacytomas are unusual causes of a sellar mass. The present case indicates that an intrasellar mass can be misdiagnosed as a macroadenoma. When treating intrasellar masses with the slightest suspicion of a non-pituitary origin, further workup should be considered. Because they have different therapeutic implications, extramedullary plasmacytomas involving pituitary gland should be considered in the differential diagnosis of a non-functioning pituitary mass.

PS2-176

Interest in treating migraine in family physicians is correlated cumulative personal exposure to migraine in themselves, their family of origin and their current household

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We wanted to know if personal history of migraine in the physician, and exposure to household members with migraine in their family of origin or current family was associated with level of interest in treating migraine patients.

In the course of analyzing migraine prescribing patterns of 32 family physicians we also obtained information by questionnaire from the physicians about their personal exposure to migraine headache. We queried them on whether they personally had migraine headache, whether they had a family member in their household of origin with migraine and whether they had a current household member with migraine.

We then constructed an index from 0-3 which we called Migraine exposure burden.

A score of zero was assigned if the physician had no exposure; a score of one was assigned if they had any of the three variables [personal history of migraine, household family of origin exposure, or current household exposure]. A score of two was assigned if they had two of these three, and a score of three was assigned if they had all three.

We found that physician interest in treating migraine was associated with a personal diagnosis of migraine at the \( P=0.008 \) level, and was associated with the cumulative exposure burden.
We conclude that personal and family first hand exposure to migraine is correlated with increased interest in treating migraine patients.

**PS2-177**

**Cephalic hypersensitivity syndromes: a new concept for chronic headache**

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**Introduction:** The number of patients suffering from chronic headache accompanied by dizziness and cephalic ringing is gradually increasing. Pathophysiology of migraine has been commonly explained by trigeminovascular theory, although recent studies have suggested that the cause of the migraine stems from cortical hyperexcitability.

The “Cortical Hypersensitivity Syndromes” is defined as a syndrome in which cortical hyperexcitability increases over time in patients suffering from long-term headache but left untreated. The primary symptoms include unilateral or bilateral cephalic ringing, insomnia, enhanced anxiety, short-term impairment of higher brain function, and daily heaviness of the head. Electroencephalogram(EEG) finding suggests widespread hypersensitivity. The syndrome can be attributed to a history of migraine, or attributed to family history within second-degree, or not attributed to another disorder.

We measured EEG in 1000 patients suffering from daily headache accompanied by dizziness and cephalic ringing.

**Conclusions:** Here we defined a new syndrome, “cephalic hypersensitivity syndrome” as a subliminal cortical hyperexcitability which itself is invisible but apparently seen as some symptoms such as dizziness and cephalic ringing. The cephalic hypersensitivity syndrome should be treated to attenuate the excitability by an appropriate triptan medication during attacks so as to exhibit its recurrence.

**PS2-178**

**Specificity in thermal pain recognition in patients with burning mouth syndrome - a fmri study**

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**Background and aim:** Burning mouth syndrome (BMS) is one of the common orofacial pain conditions with unknown etiology. Patients often feel partial alleviation of pain during meals, although response to various stimuli is not well known. This study was conducted to elucidate the difference in brain response to thermal stimulation between BMS patients and controls.

**Methods:** 18 female BMS patients and 18 female healthy controls were enrolled in this study. All subjects received thermal stimulation on right lower lip and right palm. The baseline temperature was set at 30°C and the thermal stimulation was applied in temperature at 40 and 49°C with a computer controlled Peltier device. The brain response was recorded with functional magnetic resonance imaging (fMRI) in a block design.

**Results:** Thermal stimulation on the lip resulted in brain activation in the anterior cingulate cortex, the precentral gyrus and the prefrontal cortex in the BMS patients, although it did not lead to any significant responses except for prefrontal gyrus in the control. Thermal stimulation on the palm of BMS patients activated the precentral gyrus, the superior frontal gyrus and the anterior cingulate cortex, while it induced activation of the precentral gyrus, the prefrontal cortex and the inferior temporal gyrus in the control.

**Conclusions:** Activation in the anterior cingulate cortex may be related to emotional modulation in the BMS patients. Significant brain activation after lip stimulation in the BMS patients indicates hypersensitivity in the mouth.

**PS2-179**

**The analysis of the impact of individual headache types on work activity in headache sufferers**

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Introduction: Headache is a common disorder in the working population and significantly affects overall economic productivity.

Aim: To determine the impact of individual headache types on work and work efficiency.

Methods: The study was carried out with a sample of 1022 employed persons interviewed on their work place. Through four questions and sub-questions we collected data that was statistically processed and used to analyze the effect of headache on work and work efficiency.

Results: Out of all the interviewed persons, 579 (56.65%) reported headache. Of those, 169 (16.53%) had migraine, 224 (21.91%) had tension-type headache, and 186 (19.19%) had another type of headache. The results showed that monthly absenteeism and working despite headache were most frequent in the migraine sufferers. Those working despite migraine worked less efficiently, had to make more effort, had diminished attention and precision at work and had to invest more time in accomplishing a task. The subjects suffering from tension-type headache and other headache types did not report a significant impact of their headache on the effort, attention and precision at work and the time required to accomplish a task. Work efficiency during a headache attack was 66-90% in tension-type headache sufferers, whereas in subjects suffering from other headache types it was 91-100%.

Conclusion: Headache, in particular migraine, represents a burden to patients, their families and society. It is, therefore, necessary to consider both medical and economic aspects of headache.

PS2-180
Migraine, eating behaviours and adiposity
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Aim: To determine the relationship between migraine severity and headache frequency with eating behaviours and adiposity.

Background: Recent research has highlighted an association between migraine and obesity, in adults and children. A causal relationship, and its direction, is not established. There are overlapping neurobiological mechanisms in migraine, appetite behaviour and obesity. Migraine has been noted to affect appetite behaviours, but this has not been formally studied previously. We explored the biologically plausible hypothesis that migraine may lead to obesity, via alterations of appetite, food intake and food cravings.

Method: A single-centre, cross-sectional, questionnaire-based, clinical migraine population pilot study was designed. The independent variables were migraine severity and headache frequency as determined by the pedMIDAS questionnaire. Primary dependent variables were eating behaviours (as measured by the Dutch eating behaviour questionnaire/child eating behaviour questionnaire) and body mass index (kg/m²) as a measure of adiposity. Secondary outcomes were food cravings and daily diet, evaluated by the food cravings inventory and food intake questionnaire, respectively. Exclusion criterion was prophylactic weight altering medications and non-migraine headaches. Sixty patients aged 6-16 years were recruited from tertiary neurology and general paediatric clinics. Local Research Ethics and Trust R&D approvals were granted in June 2009.

Results: Desire to drink fluids is positively correlated with migraine severity. Intake of unhealthy foods high in sugar and fat differ among different frequencies of monthly headache.

Conclusion: We demonstrate that migraines may influence thirst levels and appetite through effects on the intake of unhealthy foods.

PS2-181
Occlusion among school adolescents with tension-type headache (TTH)
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Psychosocial stress is considered to be the most predictable cause of TTH. Stress and related emotional problems almost always induce motoric reactions of facial mimic and masticatory muscles.

The aim of the study was to investigate the prevalence of occlusal dysfunctions due to an increased activity of masticatory muscles in adolescents with TTH.

Material and methods: The study comprised 207 students of a secondary school: 187 of them had TTH. The remaining 20 constituted the control group. In the TTH...
group there were 61 students with infrequent episodic TTH, 120 with frequent episodic TTH and 6 with chronic TTH. The influence of the perceived stress was evaluated using the PSS-10 Cohen’s scale. The occlusion was assessed using the T-Scan II. A contact of the opposing teeth in the maximum intercuspal position (MIP) and the centre of occlusal forces (COF) were recorded.

**Results:** Occlusal forces were mostly distributed on the teeth of the front arch in TTH students (in 83.5% of IFETTH, 92.3% of FETTH, and 100% of CTTH students). The percentage of students with moderate or strong reaction to stress depended on the TTH type (19.7% and 3.3% in IFETTH, 33.4% and 3.3% in FETTH, and 50% and 50% in CTTH students, respectively). In controls (70%), slight reaction to stress occurred.

**Conclusion:** Typically, in TTH students, occlusal forces are mainly distributed on the teeth of the front arch. COF dislocation in the direction of the front arch correlates with TTH types and the degree of the perceived stress.

**PS2-182**

**Clinical assessment of headache in patients with head trauma without loss of consciousness**

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**Aims:** All patients referred to the clinic with diagnosis of posttraumatic headache in year 2009 and 2010 underwent clinical assessment after head trauma without loss of consciousness.

**Materials and methods:** Retrospective analysis of 24 patients (16 women and 8 men), ages 18 to 75, showed that majority of patients had a history of headache (prior to head trauma), which was worsened in frequency and intensity afterward. Diagnostic criteria for headache are based upon IHS classification. Eighteen patients (75%, 13 women and 5 men) had migraine headache, four patients had tension headache, and two patients had no headache at all prior to head trauma. All patients underwent: brain MRI, which showed no abnormalities; EEG analyses, which showed either no abnormalities or nonspecific changes; and SPECT rCBF examination.

**Results:** In 22 patients (91.67%) an increase of frequency and intensity of preexisting headache was found. Lower rCBF was found in 6 patients (25%) in particular parts of the brain: in 2 patients in frontal lobe, in 3 patients in temporal lobe and in 1 patient in occipital lobe.

**Conclusion:** In most cases our patients have had history of migraine headache (prior to head trauma), and did not have posttraumatic headache, but only worsening of existing headache. In 6 patients headache has been presented with decrease of rCBF in different parts of the brain.

**PS2-183**

**New online tools to monitor migraine headache**

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**Background and aims:** A headache diary - based on the IHS classification criteria - is mandatory in research and clinical practice, given the consistent discrepancy between retrospective questionnaires or inquiry and daily state reporting. In addition, electronic diaries are more reliable than paper-and-pencil forms and when accessed safely through the internet have numerous advantages.

**Methods:** Presented are two tools to monitor migraine according to the IHS through the internet.

(1) An online headache diary with migraine monitor - a direct graphical update of headaches, IHS migraine attacks, medication use and menstruation in women per day.

(2) A real-time diary employed through smart phone, which captures migraine headache, prodromal features of migraine, and current health behavior.

This application also allows for tailored coaching of health behavior in response to the diary entry.

**Results:** The technical feasibility, acceptance and utility of both tools were successfully tested. The online diary was employed in a Dutch headache center by 28 migraine patients for 80 days at average; the neurologist used it before, within and between consultations. The real-time diary was used in 47 migraine patients with very high compliance (85-100%) and technological problems reduced to 0.5% of the entries.

**Conclusion:** Both tools are highly feasible, user-friendly and can be easily used in research and in clinical practice. In sharing these developments we intend to contribute to the issue of best practice in migraine monitoring and to the convergence in headache diary use.
Web-based self-management: current randomized controlled trial in Dutch migraine patients

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Background and aims: In order to increase the outreach of self-management training (SMT), the protocol of the face-to-face practice tested by Mérelle (2008) was modified into a web-based intervention. Advantages of online interventions include a lower threshold for seeking help, shorter waiting-lists and cost-effectiveness. In addition, diary data, homework exercises and progress of the patients are automatically stored, which facilitates monitoring and coaching. Results of the pilot study show that feasibility and acceptance are high. Both experts and new patients rated the intervention as user-friendly and captivating to work with. The intervention is currently part of a RCT, which is supported by the Dutch Headache Patients association and several Dutch Headache centres.

Methods: Web-based SMT consists of 8 lessons directed at a better view and more grip on migraine occurrence, supported weekly by a structured supportive email. Participants keep an online IHS-headache diary during SMT as well as four weeks pre-training (T1), post-training (T2) and at 6 months follow-up (T3). At T1, T2 and T3 validated questionnaires (HSLC, HMSE, MSQOL, MIDAS) are administered as well.

Results: Interest in participation in the study is high, with 400 applications between August 2010 and January 2011. Currently 160 patients are in the training and waitlist-control group. Preliminary findings suggest that effects are comparable to the face-to-face intervention. The prognosis is that 55% of patients will complete the training in time and an additional 20% completes within an extra month.

Conclusion: Preliminary findings suggest that compliance is high and the effects are promising.

Frequency rate of asymptomatic criptogenic brain infarction in female patients with primary headache

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The purpose of this study is to determine the frequency rate of cryptogenic brain infraction in female patients with primary headaches (PH).

Introduction: The share of migraine infraction in the total number of ischemic CVIs expressed in percentages is insignificant, but it is more important in patients having migraine with aura (MA) who are under 45 years old as compared to the same sex and age population without MA.

Methodology: The investigation was conducted on female patients with PH, aged 18-45, who had CT or MRI brain scanning in 2010. Patients having the anamnesis of a vascular or hematologic disease, hypertension and dyslipidemia were excluded.

Out of 185 female patients three groups were created per type of PH. 55 patients with MA were in Group I, 70 patients with migraine without aura in Group II, and 60 patients with ETTH in Group III.

Results: One or more lacunar ischemia were detected in five patients. In Groups I and II ischemia was detected in two patients each and in one patient from Group III. Further diagnostic procedures were conducted for these patients (blood tests, antiphospholipid antibody titers, ultrasound examination of blood vessels of the head and neck, echocardiography). Comorbidity relevant for ischemic CVI was detected in three patients, one from each group.

Conclusion: In accordance with the obtained results a significant difference in the frequency rate of cryptogenic brain infraction in female patients with MA as compared to female patients with migraine without aura or ETTH has not been detected.

No increased risk for atherosclerosis in migraine patients from the erf study

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**Background and aim:** Migraine, in particular migraine with aura (MA), has been associated with an increased risk of ischemic stroke and coronary heart disease. It is unknown whether this is mediated by an unfavorable cardiovascular risk profile and associated atherosclerosis. Therefore, we investigated functional and structural markers of atherosclerosis in migraine patients.

**Methods:** Subjects were participants of the Erasmus Rucphen Family (ERF) study. Atherosclerosis was assessed in 360 migraineurs (209 had migraine without aura (MO) and 151 had migraine with aura (MA)) and 617 subjects without migraine or severe headache. Atherosclerosis was quantified by Intima Media Thickness (IMT), Pulse Wave Velocity (PWV) and Ankle-Brachial Index (ABI). A large number of putative cardiovascular risk parameters and the Framingham risk scores for coronary heart disease (CHD-score) and stroke (stroke-score) were also evaluated.

**Results:** No difference was found in carotid IMT, mean PWV, or ABI between migraine patients and controls. Migraine patients had no increased odds of having an elevated CHD-score (>10%) or elevated stroke-score (>10%).

**Conclusions:** Our study shows that migraineurs have no increased risk for central or peripheral atherosclerosis. In addition, in migraine patients from the ERF population, no increased risk for stroke or coronary heart disease was observed based on classical cardiovascular risk factors. Our data suggest that classical cardiovascular risk factors and atherosclerosis are an unlikely explanation for the previously observed association between migraine and cardiovascular disease.

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**Quality of life and diagnostic transcranial magnetic stimulation in tension-type headache**

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**Background:** The pathogenesis of primary headaches possibly involves changed excitability of cortical structures which can be evaluated by method of transcranial magnetic stimulation.

**Patients and methods:** Ten patients with tension-type headache (TTH) aged 20-55 and 10 healthy age- and sex-matched volunteers were investigated. Depression (Beck Inventory), anxiety (Spielberger Inventory), quality of life (SF-36), pain intensity (100-point VAS) and results of diagnostic transcranial magnetic stimulation (TMS) were estimated.

**Results:** Patients complained of frequent (up to 2 "pain" days a week) or constant headaches mainly in evening; 4 patients with insomnia complained of morning headaches. Pain intensity (Me) was 50.00 VAS points (95%CI 39.80 - 60.10). Trait anxiety in TTH patients (Me=43.00; 95%CI 33.51 - 50.48 VAS points) was significantly higher than in healthy subjects (Me=35.00; 95%CI 32.08 - 42.11 VAS points; p=0.028). State anxiety and depression scores did not differ significantly. Statistically significant direct correlation was revealed between trait anxiety scores and pain intensity (R=0.668; p=0.034). TTH patients showed diminished quality of life, difference was significant in domains: physical functioning (p=0.010), role limitation - physical (p=0.043), role limitation - emotional (p=0.037), bodily pain (p=0.045). On diagnostic TMS a tendency to an amplitude increase was revealed in TTH patients (Me=2.40; 95%CI 1.77 - 3.08) compared with controls (Me=1.40; 95%CI 1.09 - 2.48), not reaching significance (p=0.078).

**Conclusion:** TMS changes can be regarded as a sign of increased excitability of cortex and involvement of greater cortical area in TMS answer. The difference did not reach statistical significance possibly because of small number of patients.

**PS2-188**

**All in the head? Mapping migraine on the borderland of PTSD & headache**

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**Objective:** This study aims to better understand whether Post-Traumatic Stress Disorder (PTSD) is associated with a particular type of headache by describing the prevalence of headache types experienced by a population of asylum-seekers diagnosed with PTSD.

**Background:** PTSD and migraine are both disabling conditions with significant implications for individual and public health. Studies have suggested a link between the conditions but relatively little is known about the types of headache experienced by patients with PTSD. The Horizon Centre, a GP surgery for asylum-seekers, offers the rare opportunity to study a substantial population of patients suffering both PTSD and headache.
**Method:** 82 asylum-seekers diagnosed with PTSD and with a registered complaint of headache within the past 12 months were successfully recruited to the study. Participants completed a questionnaire regarding characteristics of their headache. Results were categorised in accordance with the IHS ICHD-II diagnostic criteria to establish the relative frequency of common types of headache. Frequency data was analysed in StatsDirect, using Exact (Clopper-Pearson) 95% Confidence Intervals. Comparisons were drawn using simple linear regression models.

**Results:** 40.2% of the sample reported migraine, 15.85% tension-type headache and 2.43% cluster-like headache. A further 20.7% of respondents satisfied the criteria for probable migraine.

**Conclusion:** Migraine-like headache was the most prevalent headache type in our sample population. Comparison with worldwide prevalence estimates suggests that, among headache sufferers, patients with co-morbid PTSD are more likely to suffer a migraine-like headache. This paper calls for a greater recognition of migraine among patients diagnosed with PTSD.

PS2-180

To study the significance of dietary trigger factors and their exclusion in the aetiology and treatment of childhood headache disorders

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**Methods:** 115 Children with chronic headache (all subtypes), age range 3-15 years (mean 9.8 years) were prospectively studied in a paediatric outpatient clinic. The frequency of consumption of foods or food additives known to trigger headaches was recorded. These were: caffeine, cheese, cocoa, citrus, monosodium glutamate (MSG), aspartame and nitrates. Patients who consumed any of these foods several times a week, were advised to exclude one or two of them for 6 weeks and to record the frequency and severity of their headaches.

**Results:** 100 patients attended for follow-up. Of these 13 (13%) did not respond to dietary exclusion. 87 (87%) achieved complete resolution of headaches by exclusion of 1 (66\%\textsuperscript{th}) or 2 (21\%\textsuperscript{st}) of the identified foods. Caffeine was the most common implicated trigger (28), followed by MSG (25), cocoa (22), aspartame (13), cheese (13), citrus (10), and nitrates (6). 1 patient was sensitive only to tomatoes.

**Conclusions:** This case series demonstrates the potential scale and significance of 7 frequently consumed foods or food additives in the aetiology of chronic headache disorders in the paediatric population in this country. This study also demonstrates the effectiveness of simple, non-pharmacological treatment of chronic headache in a significant majority of children by exclusion of the identified food agent for a relatively short period of time, in a highly-motivated patient group. Further well-designed, randomised studies are needed to establish a sound evidence-base for food-related chronic headache disorders in children and adolescents.

PS2-181

Two types of medication overuse headaches divided by the relationship between the onset age of headache and insomnia

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Objectives: We investigated the relationship between the onset age of headaches and insomnia.

Background: Insomnia is one of the deterioration factors in headaches. We revealed an interesting relationship between the onset age of medication overuse headaches (MOH) and insomnia.

Methods: We studied the existence and the onset age of insomnia and the onset age of headaches using questionnaires given to 208 outpatients suffering from headaches (58 males, 150 females, with an average age of 43.1 years) in one hospital from June 2007 to November 2008. In 208 outpatients, we diagnosed 36 patients as MOH. We then determined the relationship between the onset age of headaches and insomnia.

Results: We analyzed 208 patient cases. Of these cases 131 patients had migraine (M), 110 patients had tension type headache (TH), 66 patients had both M and TH and 36 patients had MOH. Of M, 105 had insomnia, and of TH, 97 had insomnia. Then we calculated correlation coefficients (CC) between the onset age of headaches and insomnia in each type of headaches. The CC between total headaches and insomnia (0.63), between TH and insomnia (0.57) and between M and insomnia (0.41) are statistically significant. But The CC between MOH and insomnia (0.02) is not significant because of their V-shape curved distribution. We thought that MOH can be divided two groups from these results.

Conclusion: From the results of our study we suggest a possibility of the classification of MOH divided by the relationship between the onset age of headaches and insomnia.

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German “sympathico-vascular theory” for the pathogenesis of migraine

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Object: Review of the pre-World War II German articles on migraine. Background. In the German-speaking world, the pathogenesis of migraine was commonly explained by “sympathico-vascular theory”, but this theory is now ignored.

Methods: Literature survey.

Results: Du Bois-Reymond (1860) observed pallor and mydriasis during his own migraine attack, and maintained that his attack was produced by vasoconstriction due to sympathetic overactivity; he also mentioned to vaso-dilation in the later stage of his attack. Moellendorff (1867) reported dilation of the retinal artery and a transient relief of headache by compressing the carotid artery during migraine attack; this description far predated the similar famous observation by Graham and Wolff (1938). Eulenburg (1887) revealed that the majority cases of migraine accompanied vasoconstriction, while the minority presented with vasodilation, suggesting that the time of change from sympathetic overactivity to hypoactivity varied from case to case. The “sympathico-vascular theory” was supported by Flatau, Richter, Hahn, and others. Flatau (1912) explained the occurrence of headache itself by secondary exudation from blood vessels into cerebrospinal fluid (intracranial hypertension). Richter (1925) held that migraine resulted from vertebo-basilar vasoconstriction, whereas epilepsy was triggered by internal carotid vasoconstriction. Hahn (1930) wrote that transient ischemia by primary vasoconstriction induced toxic metabolic products, which might cause secondary vasodilation and exudation. Nitroglycerine and ergotamine were widely used for the prevention of migraine attack based on the “sympathico-vascular theory”; from the present viewpoint, pharmacologic properties of ergotamine include sympatholytic effect.

Conclusion: German “sympathico-vascular theory” for the pathogenesis of migraine was reasonably evidential.

PS2-193

Migraine with aura after injection of polidocanol foam in varicose veins: a familial case

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Introduction: Injection of polidocanol foam (PF) has been used as a sclerosing treatment for varicose veins. We report a familial case in which a mother and her daughter presented their typical attack of migraine with aura after PF injection.

Patients 1: A 49 years old woman affected, since the age of 25 years by migraine with aura received a PF injection for varicose veins and 2 minutes later she complained a...
blurred vision lasted 15 minutes in all visual field, followed
30 minutes later by non-migraine headache, and shortly
after by aphasia and paresthesia of the mouth and right
hand that lasted 5 minutes.

Patient 2: A 32 years old woman, daughter of patient 1,
had a typical history of migraine with aura since the age of
22, with 4 attacks per years. She received for the first time
a PF injection; twenty minutes later she referred peripher-
al blurring of vision which spread in the high part of
visual field lasting 30-60 minutes and subsequently pulsatile
headache with nausea. One week after she received a
second PF injection and after few minutes she referred
again transient blurred vision and hand’s paresthesia lasting
sixty minutes, followed by a mild headache.

Discussion: In this report we present a familial case in
which the PF injection evoked migraine with aura. The
pathological mechanism remains unknown. The respon-
sibility of a patent foramen ovale (PFO), reported by pre-
viously studies in relationship with most cases of TIA after
sclerotherapy, is been postulated.

PS2-195

Association of maternal headaches, pain
spectrum disorders and depression with teen
migraines and quality of life

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62 teens (12 to 17 years old, mean = 14.3; 44 female),
averaging 1 to 14 (mean =4) migraines (ICHD-2 criteria)
per 30 days, recruited from two outpatient headache
clinics in Columbus, OH, together with their mothers
participated in this study.

Teens completed two measurements of quality of life.
Mothers were assessed for current headache disorders,
current pain spectrum disorders, and depressive
symptoms.

Greater severity of maternal pain spectrum disorders was
associated with a greater number of teen migraine days
(r=.37, p < .005), migraine episodes per 30 days (r=.36, p <
.005), and greater severity of associated symptoms of
migraine (p=.26; p < .05) but unrelated to teen quality of
life. None of these relationships were significant when the
effects of maternal headache were controlled.

Maternal depressive symptoms were associated with
greater number of teen migraine days (r=.29, p < .05),
migraine episodes per 30 days (r=.39, p < .005), greater
severity of associated symptoms of migraine (p=.32; p <
.05) and poorer teen quality of life as measured by both

Results: The children relate more frequently than their
mothers to have had in the past at least one episode of
headache (68.7%vs52.4%,k=0.01). For all parameters, the
degree of concordance is resulted “poor” (0.001 < k <
0.20) or “moderate” (0.21 < k < 0.40). Similar correlation
values have been recognised considering the subgroup of
children with recurrent headache.

Conclusions: The low correlation obtained between
mothers and children about the prevalence of headache
and its features, leads to consider that the compilation of a
questionnaire by a single detector should not lead to an
appropriate estimate of the prevalence of headache, or to
a precise description of its features. These results allow to
explain, just partially, the high variability of the prevalence
estimates of headache. Considering our results, an “ideal”
epidemiological instrument should supply the information
received by the children and their mothers, thus allowing a
better estimate of the prevalence of headache in childhood
and adolescence.

PS2-194

Which is the true prevalence of primary
headaches in childhood?

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Background: Prevalence of recurrent headache in litera-
ture is changeable varying from 4-20% in pre-school age, to
57-82% at 15: the data vary in accordance with the diagno-
sic criteria, the methodology and the sources of detect-
tion. Therefore we assessed the concordance between
mothers and children reporting the characteristics and
the frequency of headache, by the compilation of an ana-
mnestic questionnaire.

Method: We have recruited a non-clinical sample made
up of 425 children (average age 9.58±0.2). The question-
naire given to the children has been carried out individually
by a clinical expert, while the mothers have answered the
questionnaire independently.
Maternal depressive symptoms remained significantly related to teen quality of life when the effects of maternal headache were controlled for.

The relationship between teen headaches and mother’s pain disorders was largely explained by the effect of maternal headaches. However, maternal depression appeared to make a contribution to quality of life in teens that was independent of maternal headaches or comorbid pain spectrum disorders.

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**PS2-196**

**Headache in patients with multiple sclerosis, a cross-sectional study**

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**Objective:** To determine the prevalence of different types of headache in Multiple Sclerosis (MS).

**Background:** One of the controversial ideas concerning MS is its relationship with headache. However headache hasn’t been recognized as a symptom of MS and it is not clear whether MS causes headache or not.

**Methods:** We studied 201 patients with definite diagnosis of MS in a tertiary MS Clinic. For every patient a questionnaire was filled to obtain information about the disease and their experience of headache.

**Results:** From the total 201 patients, 48 male and 153 female, 61.2% were diagnosed with relapsing-remitting MS (RRMS) and 8.95% with primary progressive MS (PPMS), 23.9% with secondary progressive MS (SPMS) and one with progressive MS with relapse. 45.8% were suffering from headache, including migraine in 18.4%, tension in 25.4% and trigeminal neuralgia in 1.5% of cases. One case had cluster headache. The prevalence of headaches was 52.8% in RRMS and 27.7% in progressive types of MS, (P= 0.001).

In patients with positive history of headache, 18.5% (17 out of 92 patients) reported headache as one of presenting symptom of MS. In 14% of RRMS patients with headache, sometimes it preceded attack.

The prevalence of headache was significantly different in patients on interferon compared to the others (55.2% vs. 33.3%). (P=0.002)

**Conclusion:** The prevalence of headache is significantly higher in patients with MS, more prevalent in RRMS and it may be a presenting or warning symptom of an attack. Interferon therapy could be an inducer or aggravator of headache.

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**PS2-197**

**Use of the acupuncture in the treatment of tension-type headache**

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**Background and aims:** The effect of the acupuncture on the pain intensity of the patients having tension-type headache was investigated.

**Method:** 80 patients aged from 18 to 55 (51 females and 29 males) having tension-type headache were observed. The pain was examined and measured according to the visual analogue scale (6-7 points). All patients were observed (MRI etc.). The patients were divided into two groups. The first group (62 patients) received in addition their basic medication and acupuncture (GI 4, GI 11, E 36, RP 6, P7, MC 6, TR 5, F 2, IG 3, T 12-18, T 20, IG 10, IG 12-15, GI 14-16, V 7-15, VB 19-21, VB 3-9, TR 17, TR21-23, VBI, V 2-6, VB 14-16, T 22-24). The complete course was 10 - 12 procedures. The second group (control, 18 patients), received only the basic medication.

**Result:** The pain intensity of the patients in the first group was reduced after 6 - 7 days of treatment (96.7% patients) compared to the control group, where pain reduction after 12 - 16 days of treatment (44.4% patients); p < 0.01.

**Conclusion:** The addition of the acupuncture to the treatment of tension-type headache resulted in earlier remission.

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**PS2-198**

**Assessment of personality disorders in headache patients**

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**Background:** Part of the burden of headaches is produced by the psychiatric conditions that occur in...
association with them. A thorough personality assessment of the headache patients may have implications for diagnosis and treatment.

**Methods:** An ongoing study of personality assessment is conducted among patients of our Headache Center. The diagnosis follows the criteria of the IHC. All patients undergo an examination by a psychologist. For the assessment 4 scales are used: the Cognitive Behavioral Assessment for Evaluation of Outcomes (CBA-VE), the Eysenck Personality Questionnaire Revised (EPQ-R) short scale version, the Somatization Scale from the SCL-90R (SOM), and a generic scale for the study of self-esteem (SES).

**Results:** So far 23 patients (20 W and 3 M) were examined. Mean age was 38,1 ± 12,2 years. The patients revealed pathological scores in the dimensions of anxiety (21,6 ± 13,9), welfare (24,6 ± 11,1) and positive change perception (22,4 ± 6,6) of the CBA-VE, in the SOM (1,2 ± 0,9), and in the SES (8,2 ± 4,1).

**Conclusions:** Although these patients do not suffer for major psychiatric disorders, however show anxious comorbidity with aspects of somatization. They have low perception of welfare, do not present a positive change perception, and have low levels of self-esteem. The lack of pathological findings at EPQ-R could indicate that they live in an apparent “normality mood”. Headache could be interpreted as “alert bell” of an underlying personality disorder; therefore it is important to investigate comorbid psychiatric conditions in headache study to formulat treatment plans.

**PS2-199**

**Combination analgesic prescribing: a drug utilisation study**

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**Background and aims:** The South African analgesic market contains a large number of combination (polycomponent) analgesic products. The potential for abuse of combination analgesics is high. The primary aim of the study was to determine the extent and pattern of combination analgesic prescribing in a South African patient population and to compare the results with previous studies.

**Methods:** A retrospective, cross-sectional drug utilisation study was conducted. Computerised medication records were obtained from a large prescription database of a medical aid administrator in South Africa. The database contained 2126264 records for medication and procedures for 2010.

**Results:** A total of 146800 analgesics were prescribed at a total cost of R4593162. Combination analgesics with either paracetamol or aspirin as the main active ingredient accounted for 64.95% of analgesic prescriptions, single component analgesics and antipyretics for 24.04%, narcotic analgesics for 6.93% and other analgesics for 4.09%. Combination analgesics comprised 72.00% of the cost of analgesics. Most combination analgesic trade name products were available as tablets and the majority of products contained paracetamol as main constituent. Most products also contained codeine phosphate which has addictive potential. Some combination analgesics had exactly the same dosages of active ingredients but were marketed under different trade names. The most frequently prescribed trade name product, accounting for 13.48% of prescriptions, consisted of ibuprofen 200mg, paracetamol 350mg and codeine phosphate 10mg.

**Conclusion:** Findings were generally in agreement with those of previous South African studies. Further studies, including qualitative studies and studies on dosages, are recommended on combination analgesic prescribing.

**PS2-200**

**Personality profiles in chronic and episodic migraine**

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**Background and aims:** Recent literature shows association between personality traits and chronic headache and medication overuse headache. However studies comparing chronic and episodic migraine with healthy controls in terms of personality traits are limited.

**Methods:** Patients were evaluated for migraine frequency, duration, severity, gender, medication overuse, education level, comorbid systemic diseases, psychiatric disorders and personality. We used Beck depression inventory to evaluate depression, minipsychiatric interview for psychiatric evaluation and The Minnesota Multiphasic Personality Inventory(MMPI) for personality profiles.
We compared chronic and episodic migraineurs with healthy individuals.

**Results:** There were 31 chronic migraine patients, 29 episodic migraine patients and 23 healthy individuals. There were no differences in gender, education level and age between groups. Variance analysis revealed hypomania (HYN), paranoia (PAR), depression (DEP), hysteria (HYST) and hypochondriasis (HYP) scales of MMPI were significantly different between groups. Episodic headache patients and control group were significantly different in HYN, HYST, DEP, HYP scale scores. Chronic headache patients with medication overuse were significantly different from control group in HYP, PAR, HYST, HYP scale scores. There were no differences in MMPI scores between chronic headache patients with or without medication overuse. Beck Depression Inventory scores were significantly different between medication overuse patients and episodic headache patients and also between healthy individuals and episodic headache patients.

**Conclusions:** Our results demonstrate that there are differences in personality profiles of healthy individuals, episodic migraine patients and chronic headache patients with or without medication overuse.

**PS2-201**

**Poor sleep in migraine is related to migraine aura and attack frequency; report from lumina**

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**Background:** Sleep disturbances are a common and burdensome complaint in migraineurs, and have been identified as a precipitating factor of migraine attacks. Conversely, sleep is an important relieving factor for migraine in a subset of patients. Previous literature suggests that one-third to one-half of headache sufferers have chronic sleep difficulties, but few studies have focused on subjective sleep quality in a large cohort of migraineurs.

**Methods:** We sent out a digital questionnaire on migraine and sleep to 2,877 self-reported migraineurs from the LUMINA-database. The questionnaire included a.o. the Munich Chronotype Questionnaire (MCTQ) and items on attack timing. Chronotype was assessed with a seven-level MCTQ-question on self-reported chronotype, for all migraineurs, and subtypes with (MA) and without aura (MO). Relations between chronotype and attack timing were analysed using chi-square tests.

**Results:** A total of 2,374 (82.5%) migraineurs participated with a mean age (SD) of 45.0 (11.6) years. Mean PSQI total score (SD) was 6.5 (3.6), and 1.275 (35.5%) of migraineurs had a PSQI total score >5, indicating poor sleep quality. Poor sleepers were older (p < 0.001); more frequently female (p < 0.001); had higher BMI (p < 0.001) and had higher HADS-score (p < 0.001). Regression showed higher age (p < 0.001), female gender (p < 0.001), higher attack frequency (p < 0.001) and higher HADS-score (p < 0.001) were predictors for poorer sleep quality, whereas MO (p = 0.036) was related to better sleep quality.

**Conclusion:** Over 50% of migraineurs report poor sleep quality. Furthermore, MA and higher attack frequency are related to poorer sleep quality.
differences between MO and MA (p=0.46). Over 60% (n=1,424) reported specific circadian timing of migraine attacks, with n=495 (20.9%) between 0:00-6:00am, n=449 (18.9%) between 6:00-12:00am, n=387 (16.3%) between 12:00-6:00pm, and 93 (3.9%) between 6:00-12:00pm. Attack onset differed between chronotypes (p=0.001); early attack onset (0:00-6:00am) was most prevalent in ‘extreme early’ (30.6%), whereas late onset (6:00-12:00pm) was most prevalent in ‘extreme late’ chronotypes (5.8%).

Conclusion: Chronotype distribution among migraineurs is shifted to ‘moderate early’ and ‘moderate late’, when comparing to the general population. Early morning attack initiation is most prevalent, and circadian timing of attack onset differs between chronotypes.

PS2-203
Global perceived effect (gpe) and headache impact test (hit-6) scores in a naturalistic headache clinic setting
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Objective: To assess the clinical outcome of patients with migraine, tension type headache (TTH) and medication-overuse headache (MOH) by means of the Headache Impact Test (HIT-6) score and the Global Perceived Effect (GPE).

Methods: Patients attending a headache clinic who were diagnosed as TTH, migraine or MOH and of whom follow-up data were available were prospectively included. All patients completed a HIT-6 questionnaire at baseline and on follow-up; the clinical outcome on follow-up was assessed by means of the GPE. GPE data were dichotomized into improved (slightly, moderately or strongly) and not improved on follow-up (stable or worse clinical condition).

Results: 251 patients (167 migraine, 53 TTH and 31 MOH) were included. Mean follow-up was 11.5 +/- 9.7 weeks. Mean HIT-6 score on baseline was 64.7 +/- 6.6. A favorable clinical evolution (GPE) was seen in 192 patients (76.5%). HIT-6 score on follow-up was 60.9 +/- 6.6. Of those patients with a favorable clinical evolution, the HIT-6 score on follow-up was 59.9 +/- 6.2. Still 53% of patients with a favorable clinical evolution had a HIT-6 score on follow-up above 60, meaning that headache interferes strongly with activities of daily living.

Conclusions: More than 75% of patients visiting a headache clinic have a favorable clinical evolution. However, approximately half of the patients with an assumed favorable clinical evolution still have headaches that strongly interfere with daily life. The latter could lead to medical shopping, headache chronification and medication overuse.

PS2-204
The typical duration of migraine aura: a systematic review
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Background: In the absence of diagnostic markers a detailed history of symptoms is crucial when diagnosing migraine aura (MA). In the ICHD-II, non-hemiplegic migraine aura (NHMA) duration is considered normal when between 5 and 60 minutes whereas hemiplegic migraine aura can be longer. In our experience NHMA symptoms often continue beyond one hour time.

Methods: We performed a systematic literature search identifying articles pertaining to a typical or prolonged duration of NHMA. We also performed a comprehensive literature search in order to identify all population-based studies or case studies/series where clinical features of NHMA, including but not restricted to aura duration, were reported, in order to gain a complete coverage of the available scientific data about aura duration.

Results and discussion: We did not find any article exclusively focusing on prolonged aura or more generally on MA duration. We found thirteen articles where MA features were investigated, including the aura duration. Five articles recorded the overall duration of NHMA, which lasted for more than one hour in 11.6% - 31% of patients. Four articles reported the prevalence of individual NHMA symptoms lasting for more than one hour: visual aura lasted for more than one hour in 6%-10% of patients, sensory aura in 14-27% of patients and aphasic aura in 17-60% of patients.

Conclusions: This systematic review indicates the maximum duration of NHMA may be longer than currently reflected in the ICHD-II criteria. This seems to be especially true for non-visual aura symptoms.
PS2-205

Headache in three new cases of harlequin syndrome

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Background and aim: Harlequin syndrome (HS), first described by Lance and colleagues (1988), is a rare autonomic disorder characterized by unilateral diminished sweating and flushing of the face in response to heat or exercise. Some patients with HS complain of headache.

Methods: We present three new HS cases particularly to characterize their headache phenotype.

Results: The patients were female, aged 69, 58 and 42 years, who during an exercise noted than one side of their face became red and sweaty while the other side remained white and cold. The neurologic examination was uniformly normal; no asymmetric facial flushing or sweating was noted at rest. They had neurological, radiological, autonomic and cardiovascular investigations, which did not show any pathological findings. These are typical idiopathic cases with a benign natural course, as illustrated two patients having an essentially stable eighteen year course. Two out of three presented episodes of unilateral headache associated with exercise: in one case the headache had migraine features and was contralateral to the side where the flushing occurred, whereas the second patient, who had had migraine attacks in the past, suffered from a brief throbbing headache without any other associated symptoms, ipsilateral to the facial flushing. The third woman did suffer from migraine but the attacks were not associated with HSG. She had many pharmacologic tests, included a nitroiglycerin challenge that did not induce any flushing but provoked migraine.

Conclusions: These data do not show a strong correlation between the phenotypic expression of migraine and HS.

PS2-206

Migrainous infarction: a complication of familial hemiplegic migraine in a child

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Background and aim: Migrainous infarction (MI) is a complication of migraine with aura. While MI is more recognized in adults, reports in childhood are rare. We describe a child with familial hemiplegic migraine and migrainous infarction.

Methods: Clinical presentation, neuroradiologic findings and outcome are reported.

Results: A 10 year old boy whose mother has hemiplegic migraine developed left hemiparesis preceded by right sided headache, left sided paresthesia, photophobia and phonophobia. On admission, brain MRI, MRA and CTA of the carotids and circle of willis were normal. All symptoms resolved within 3 hours of onset. Two more similar episodes lasting 45-60 minutes occurred within the next week after initial onset for which he was started on Verapamil. Eight days after the initial episode, he again developed headache and left hemiparesis. Headache resolved within 24 hours but hemiparesis persisted. Repeat brain MRI and MRA showed acute infarct in the right putamen and globus pallidus with decreased caliber of the right ICA and M1 segment. ECHO and EEG were normal. Hypercoagulable work-up did not show a prothrombotic disorder. Genetic mutation testing for hemiplegic migraine was negative. He was treated with ASA, clopidrogel, verapamil and magnesium. After 10 weeks of intensive rehabilitation followed by outpatient therapy, he made significant recovery with only mild residual deficits. Repeat CTA 3 months after onset showed significant improvement of right ICA and M1 stenosis without collateral formation.

Conclusion: This case illustrates the occurrence of migrainous infarction in childhood and emphasizes the need for early recognition and treatment.

PS2-207

Interaction between anxiety and cortical excitability in migraine children: a neurophysiological and psychological study

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Background and aims: Migraine is a common neurological condition in children and adolescents causing a significant impact on quality of life. Previous studies in migraineurs showed a correlation between neurophysiological abnormality and emotional symptomatology. Aim of this study was to characterize the correlation between neurophysiological and psychological data, concerning both internalizing and externalizing behavioral disorders.

Methods: We compared the auditory P300 potential habituation in 12 patients (mean age: 10.8±1.4 years) affected by migraine without aura and 10 control subjects (mean age: 11.8±2.5 years). P300 response was recorded in three successive blocks to test its amplitude reduction from the first to the third block. As for the externalizing problems, response to frustration was assessed by means of the Picture Frustration Study (PFS), while the internalizing symptoms were investigated by means of the ‘Scale psichiatriche di autosomministrazione per fanciulli e adolescenti’ (SAFA) questionnaire for anxiety and depression.

Results: P300 habituation was lower in migraine children than in control subjects (F=8.31, p=0.005). In migraineurs, a significant positive correlations between the P300 habituation deficit and the total anxiety SAFA score was found (p=0.02), while the P300 reduced habituation did not interact with the PFS scores.

Conclusions: This is the first study showing a correlation between a neurophysiological abnormality (reduced P300 habituation), probably related to abnormal brain excitability, and anxiety in migraine. These results suggest that both neurophysiological abnormalities and psychological tracts concur in determining the migraine phenotype in childhood.

PS2-208
Incidence and risk factors of chronic daily headache and its subtypes in adolescents
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Background and aims: The scope of chronic daily headache (CDH) in adolescents is not well defined. This study investigated its incidence rate and relevant risk factors.

Methods: A field cohort of adolescents aged 13 to 14 was established in three middle schools in Tai-Tung County, Taiwan for three consecutive years. Participants without CDH at baseline were annually followed up for one or two years. At baseline and follow-ups, each participant completed the same questionnaires including sociodemographics, headache profiles, Adolescent Depression Inventory and Pediatric Migraine Disability Assessment (PedMIDAS). Potential new-onset cases of CDH were interviewed by neurologists and also finished one-month headache diary for diagnostic ascertainment. Incidence rates of CDH and its major subtypes (chronic migraine (CM) and chronic tension-type headache (CTTH)) and relevant risk factors were calculated.

Results: The incidence cohort consisted of 3,342 adolescents and completed 5,586 person-years of follow-up. Sixty-three subjects (21M/42F) developed new-onset CDH with an incidence rate of 1.1% person-years. Of them, 28 had CM (0.50% person-years) and 31 had CTTH (0.55% person-years). Four CDH subjects (6%) reported moderate or severe disability (PedMIDAS score≥31). Overall, 45 subjects (71%) had baseline or current diagnosis of migraine. The independent risk factors of CDH incidence included female gender, baseline low economic status, high depression score and high headache frequency. The risk factors for CM and CTTH were similar.

Conclusion: New-onset CDH was not uncommon in young adolescents. Most adolescents with new-onset CDH had a migraine history. The incidence rates and risk factors of CM and CTTH were similar.

PS2-209
Headache types, work up and attitudes toward treatment among Pakistani patients
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Background and objective: The aim of this study was to characterize headache patients with regard to classification, presentation and attitudes toward treatment among Pakistani patients.

Methods: Prospective data collection at three centers in Pakistan during 2009 and 2010. Headache classification was based on International classification of headache disorders (ICHD-2). Diagnosis was confirmed by a neurologist trained in headache diagnosis and treatment.

Results: A total of 970 patients (683;70% women) were included in study. Mean age of patients was 33±14 years.
Out of these, Frequency of headaches as reported by patients were constant (279; 29%), daily (221; 23%), 2-3 times a week (253; 26%) and 3-4 times a month (124; 13%) while 93 (10%) had infrequent headache. 414 (943%) patients had a close family member with history of headache. 98 (10%) visited a hospital emergency room for severe headache. Migraine; 487 (52%) was most common type with 39 (4%) were Migraine with aura, 12 (1.5%) were Migraine with complications while 436 (45%) were Migraine without aura. Other common headache types included Tension type headache; 350 (37%), Mixed Migraine and TTH; 58 (6%), Cluster headache; 8 (1%). Only 13 (1.5%) patients were receiving Triptans, 118 (13%) were taking migraine prophylaxis, 167 (18%) were taking injectables for recurrent severe headaches while rest were taking Paracetamol or various non-steroidal analgesics.

**Conclusion:** Migraine and tension type headaches are most common headache types. More than 52% patients had daily or constant headache. Majority of patients with Migraine were not receiving Triptans or migraine prophylaxis.

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**PS2-210**

**Evaluation of cognitive function in migraine patients - a study using event-related potential**

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To clarify the neurophysiological mechanism of cognitive impairments in migraine patients, we evaluated the relationships between event-related potentials (ERPs) and various behavioral data such as performance, subtype, severity, duration, and usage of preventive medicine. Thirty one patients suffering from migraine without and with aura were enrolled in headache-free periods. Severity of the headache was assessed by headache impact test-6 (HIT-6). Two tones counting auditory oddball paradigm was used for the ERPs. EEG was recorded from 20 channels on the scalp and recomputed global field power (GFP) from the all channel. We assessed counting performance and the P3 GFP peak amplitude and latency. Forty four percent of patients (n=15) were classified into the good performance group. There were no differences in age, usage of prophylactic drug, the presence or absence of aura, score of HIT-6, and P3 parameters between the good and poor performance groups. The group of long duration showed decreased P3 GFP peak amplitude and HIT-6 score. The group with preventive medicine significantly had more attacks of the month than the non-medication group. In addition, this group showed prolonged P3 GFP peak latency and decreased P3 GFP peak amplitude. These findings suggest that ERPs abnormalities may reflect abnormal information-processing for the attention preceding target recognition in migraine patients.

**PS2-211**

**Complementary and alternative medicine use among u.s. Adults with migraines/severe headaches**

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**Objective:** While many patients with chronic conditions use complementary and alternative medicine (CAM), little is known about CAM use by adults with migraines/severe headaches. Our objective was to determine patterns, reasons for, and correlates of CAM use by U.S. adults with migraines/severe headaches.

**Methods:** We compared CAM use between adults with and without self-reported migraines/severe headaches using the 2007 National Health Interview Survey (n=23,393), a national cross-sectional survey.

**Results:** Adults with migraines/severe headaches used CAM more frequently than those without (49.5% vs. 33.9%, p<0.0001); differences persisted after adjustment (adjusted OR=1.29, 95% CI [1.15, 1.45]). Mind-body therapies (e.g., deep breathing exercises, meditation, yoga) were used most commonly. More than 50% of adults with migraines/severe headaches reporting CAM use had not discussed it with their health care provider. Nonetheless, those with migraines/severe headaches used CAM more often than those without because of provider recommendation and because conventional treatments were perceived as ineffective or too costly. Correlates of CAM use among adults with migraines/severe headaches included anxiety, joint or low back pain, alcohol use, higher education, and living in the Western U.S. Only 4.5% of adults with migraines/severe headaches reported CAM use to treat their migraines/severe headaches.

**Conclusions:** CAM is used more often among adults with migraines/severe headaches than those without. However, few report using CAM to specifically treat migraines/
severe headaches. Mind-body therapies are used most frequently. Further research is needed to understand the effectiveness and mechanisms of CAM treatments in adults with migraines/severe headaches.

PS2-212

Validation of a diagnostic web-based cluster headache questionnaire

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Background: For large scale genetic studies in cluster headache (CH) interviewing all participants is very time consuming and self-administered, validated web-based questionnaires are needed.

Objective: To validate a web-based questionnaire to diagnose CH and to develop and validate a new prognostic model.

Methods: Of 962 self-reported CH patients who filled out our web-based CH questionnaire, 291 underwent a semi-structured telephone interview to confirm the diagnosis. Sensitivity, specificity, positive (PPV) and negative predictive values (NPV) were calculated with the telephone diagnosis as golden standard. Logistic regression with stepwise forward selection was used to create a prognostic model in a randomly selected sample consisting of 80% of the total sample. A Receiver Operating Characteristics (ROC) curve was made to define the optimum cut-off point for the diagnosis of CH with regard to sensitivity and specificity. The derived prognostic model was validated in the remaining 20% sample.

Results: Our questionnaire proved to have a sensitivity of 70.4%, a specificity of 70.8%, a PPV of 92.4% and an NPV of 32.1%. Using logistic regression, six predictor variables were selected in the 80% sample consisting of 80% of the total sample. A Receiver Operating Characteristics (ROC) curve was made to define the optimum cut-off point for the diagnosis of CH with regard to sensitivity and specificity. The derived prognostic model was validated in the remaining 20% sample.

Conclusion: We propose to use the 6-item questionnaire to select self-reported CH patients for large sample collection for research purposes.

PS2-213

Cluster headache: a prospective follow-up study on the relation between life style habits and disease course

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Background: Cluster headache (CH) has often been associated with lifestyle habits such as smoking and alcohol use. To determine whether lifestyle habits play a role in the evolution of episodic- (ECH) and chronic CH (CCH) we performed a prospective follow-up study in 812 CH patients.

Methods: In 1993, as part of a Dutch nation wide CH study, patients filled in questionnaires and were included according the International headache society criteria for CH. Four to seven years later, a follow-up questionnaire inquired about (i) the course of CH, (ii) certain lifestyle habits (smoking and the use of alcohol and coffee), and (iii) a history of obstructive sleep apnea (OSA)-like symptoms, head trauma and meningitis. Patients who changed from one CH category to another (ECH â†’ CCH) were compared with those who had not changed and the differences in the lifestyle habits and other factors were analyzed.

Results: Of 634 patients diagnosed as ECH at baseline, 3.5% had evolved into CCH and 35% of 178 patients CCH had evolved into ECH. We found that smoking was significantly related to remaining chronic in the PCCH group. We also found a significant relation of head trauma in CCH women with maintaining their chronic course.

Conclusion: We conclude that smoking was related to remaining chronic in PCCH patients and a head trauma to remaining the chronic course in CCH women.

PS2-214

Migraine with aura and the metabolic syndrome: a prospective cohort study

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Background: Migraine with aura has been found to be a risk factor for cardiovascular disease including ischemic stroke and myocardial infarction. The mechanism underlying this comorbidity is unclear. It has been suggested that migraine is associated with the metabolic syndrome.

Methods: Two large population-based cohort studies were conducted 11 years apart in the Nord-Trøndelag Health Study in Norway (HUNT-2 and HUNT-3), in which 42,407 and 30,821 subjects (>20 years) respectively, participated in a health examination and could be classified according to headache status. 17,049 subjects who participated in both studies could be assessed for the development of metabolic syndrome.

Results: In adjusted multivariate analyses migraine with aura was associated with a higher prevalence of metabolic syndrome in both HUNT-2 (OR 1.37, CI 1.06-1.76) and HUNT-3 (OR 1.37, CI 1.19-1.57) when compared to headache-free controls. Prospective analysis showed that those who had migraine with aura had a substantially increased risk for developing metabolic syndrome over the following 11 years when compared to controls (RR 1.90, CI 1.40-2.58), while a moderately increased risk was seen for migraine without aura (RR 1.26, CI 1.07-1.48) and non-migrainous headache (RR 1.21, CI 1.09-1.35). Smoking and physical inactivity were independent risk factors for developing metabolic syndrome, but in those who had migraine with aura they conferred a particularly high risk.

Conclusions: Migraine with aura is associated with a high prevalence of metabolic syndrome, and is an independent risk factor for developing metabolic syndrome. The risk is modified by lifestyle factors.

PS2-215
The effects of progressive muscle relaxation on sleep in patients with migraine - results of a randomized controlled study
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Background: Progressive muscle relaxation (PMR) is recommended for migraine as well as for insomnia. Evidence is limited and a randomized controlled study on PMR in migraine prophylaxis recently performed in our center failed the primary endpoint, i.e. reduction in migraine days. In this study we analysed the effect of PMR on subjective sleep variables.

Patients and methods: We included 123 patients with migraine without aura and migraine with aura according to ICHD-II. Patients were randomly assigned to a professionally guided PMR group therapy or a waiting group. Patients were advised to perform PMR at home every day. The study duration was 28 weeks including 4 weeks of baseline, 6 weeks of therapy and 18 weeks of follow-up. All patients kept a headache diary and completed the Pittsburgh Sleep Quality Index (PSQI) at baseline and in week 6, 12, and 24.

Results: In the treatment group, sleep quality (p=0.038), sleep-onset latency (p=0.017) and total PSQI score (p=0.022) had improved significantly after 6 weeks of PMR training. The number of PMR exercises showed a significant positive influence on subjective sleep quality (p=0.013), sleep-onset latency (p=0.009) and total PSQI score (p=0.002). These improvements, however, did not persist throughout further follow-up. In the waiting group, there were no statistically significant changes.

Conclusion: This is the first study showing that PMR leads to a significant short-term improvement of subjective sleep quality and a decrease of sleep-onset latency in migraineurs. The improvement of sleep parameters was significantly associated with the number of PMR exercises.

PS2-216
Idiopathic intracranial hypertension (IIH) - persistence of headache despite no signs of active disease
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Background and aims: IIH is a condition of raised intracranial pressure (ICP) in the absence of identifiable secondary cause. It primarily affects young obese females and potentially causes visual loss and chronic disabling headache. We aimed to examine relapse rate and long-term outcome in IIH patients.

Methods: A prospective controlled study of 17 newly diagnosed IIH patients followed for a mean period of 20 months. Baseline and follow-up included ophthalmological
and neurological examination and a detailed history of headache. Relapse was defined as recurrence of either: 1) papilledema or 2) symptoms and raised ICP.

Results: Relapse was found in 29%. Visual function improved from baseline to follow-up and was generally favorable. Headache was still present in 71% of the patients but generally with reduced intensity and frequency compared to baseline. Headache was heterogenic and unrelated to signs of raised ICP.

A weight loosing program was initiated at baseline, but no significant change in overall BMI was seen at follow-up. Weight increased in the relapse group compared to reduced or stable weight in the non-relapse group (p = 0.02).

Conclusions: While visual outcome was favorable headache was a persistent symptom. The headache was difficult to classify and was equally represented in the relapse and non-relapse group. Headache is thus a poor marker of active disease. Central sensitization of supraspinal pathways might explain why headache is not reversed with ICP normalization. The high recurrence rate emphasizes the importance of detailed and long-term follow up for years after initial remission.

PS2-217
The prevalence and burden of primary headache disorders in China: a population-based door-to-door survey
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Background: In the absence of reliable data on the prevalence and burden of primary headache disorders in the mainland of China, a population-based survey was initiated by Lifting The Burden: the Global Campaign against Headache.

Methods: Throughout all regions of China, 5,041 non-related adult respondents aged 18-65 years were randomly sampled from the general population according to the EPI method established by WHO, visited by door-to-door calling and surveyed using the structured questionnaire developed by Lifting The Burden, translated into Chinese and adapted to Chinese culture after a pilot study.

Results: The estimated 1-year prevalence of primary headache disorders was 23.8% (95% CI 22.6-25.0%); of migraine 9.3% (95% CI 8.5-10.1%), of tension-type headache (TTH) 10.8% (95% CI 9.9-11.6%) and of chronic daily headache (CDH) 1.0% (95% CI 0.7-1.2%). Of respondents with migraine, TTH and CDH, moderate or severe impact and therefore high need for effective medical care were reported by 38.0%, 23.1% and 47.9% respectively. The WHOQoL-8 questionnaire showed all three types of headache reduced life quality. The total estimated annual cost of primary headache disorders, including migraine, TTH and CDH, was CNY 667.9 billion, accounting for 2.22% of GDP (direct cost: CNY 104.0 billion, 0.35% of GDP; indirect cost: CNY 563.9 billion, 1.88% of GDP).

Conclusions: The prevalence of primary headaches is high in China, and not dissimilar from world averages. These headaches cause disability, impair work, study and daily activities, decrease life quality and bring about a heavy and hitherto unrecognized socioeconomic burden.

PS2-218
Clinical characterization of tension-type headache in the neurological clinic of a university hospital in China
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Objective: To investigate the clinical characteristics and the pattern of diagnosis and treatment of patients with tension-type headache in a tertiary neurological outpatient setting.

Methods: A cross-sectional study was conducted in the neurologic clinic of the First Affiliated Hospital of Chongqing Medical University from March through May 2010. All patients with the primary complaint of headache were interviewed by physicians face-to-face. A questionnaire collecting data of each headache patient was fulfilled by physicians and headache diagnosis was made according to the ICHD-2.
Results: A total of 1806 patients with headache complained were interviewed. Among them, 1683 responded to the questionnaire with a 93.2% response rate.

Total sums of 399 patients were diagnosed to have tension-type headache, and the mean age was 44.8 ±12.8 years. 66.9% were female patients. 44.9% of the patients were diagnosed as suffering from chronic tension-type headache. 63.7% of the patients described their headache quality to be swelling.

Of all tension-type headache sufferers, 64.9% had consulted a physician in the year before, and only 22 patients (5.5%) had been diagnosed previously as tension-type headache by physicians. 41.4% of the patients had already taken analgesic for acute treatment, and 13.3% of them were considered having medication overuse. No patient had ever received prophylactic medicine.

Conclusion: Many patients with tension-type headache neither received an appropriate diagnosis nor effective treatment. Tension-type headache remains underrecognized in China. In order to improve the situation, the authors recommend that both physicians and patients should be better educated about the tension-type headache.

PS2-219

Headache profile in 20 patients with hypertrophic cranial pachymeningitis

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Background: Hypertrophic cranial pachymeningitis (HCP) is a rare disease due to localized or diffuse thickening of the duramater. While headache is the most common manifestation, the clinical characteristics of the headache in HCP have not been well characterized in larger samples.

Methods: From 2006 to 2010, twenty consecutive patients with HCP presenting with headache were reviewed (12 women, 8 men; mean age: 43 years). Diagnosis was based on characteristic neuroimaging findings.

Results: One side of head was affected in 5 patients and both sides in 15. The characteristics of headache was presented swelling pain (n=4), stabbing(n=2), pulsating (n=1), dull(n=1), tight(n=1), lancinating(n=1), swelling and pulsating(n=3), swelling and stabbing (n=3), sharp and lancinating(n=1), undescrptive (n=3); Headache was epidodic in 5 patients and persistent in 15. The degree of headache in all patients was moderate-severe. Patients had associated nausea and/or vomiting(n=5), vomiting and blury vision(n=1),nausea and tearing(n=1), nausea, vomiting, phonophobia and photophobia(n=1), ipsilateral conjunctival injection and tearing(n=1). 9 had not any associated symptom. Chronic daily headache(CDH) was the most common headache pattern observed, including new daily-persistent headache(n=8), chronic tension-type headache(n=4), chronic migraine(n=2) and hemicrania continua(n=1). Headache was only symptom in 9 patients. Headache interfered with sleep in 16 patients. MRI of head was normal in 7 patients but all patients displayed hyper trophyed duramater with marked enhancement after Gd-DTPA administration.

Conclusion: The headache of HCP is often typically a CDH. Gadolinium-enhanced MRI should be considered in the differential diagnosis of refractory CDH with or without associated cranial neuropathy or other associated neurologic deficits, especially the headache disturbs sleep.

PS2-220

Cardiac cephalalgia - pilot study in post coronary care unit

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Cardiac cephalalgia, coded as 10.6 by ICHD-II, is secondary headache that develops concomitantly with acute myocardial ischaemia and resolves without recurrence after effective medical therapy for myocardial ischaemia or coronary revascularisation. According to literature data, cardiac cephalalgia, with only 35 cases reported, is rare headache disorder.

The aim of this pilot study was to estimate the frequency and clinical features of cardiac cephalalgia in patients with recent myocardial ischemia.

The study was conducted on 50 patients with diagnosed myocardial infarction or attack of angina pectoris hospitalised in post coronary care unit. The data about coronary disease were collected from medical records and the questionnaire designed according the ICHD-II criteria for cardiac cephalalgia. The patients were interviewed three days after admission.
Five (10.0%) patients, aged 46–64 years, all males, had cardiac cephalalgia. Headache preceded chest pain from two months to seven days in three patients and developed concomitantly with chest pain in two of them. The intensity of head pain were moderate, but it exceeded the intensity of chest pain in one patient. Non-pulsating quality and lack of associated symptoms were noted in four patients. None of these patients had headache previously and actual headache resolved after thrombolytic treatment in all patients.

According to results of our study, cardiac cephalalgia is not a rare headache disorder. The further investigation in the settings of post coronary care unit should provide more details about this secondary headache.

**PS2-221**

**How do general practitioners treat their migraine patients? Use of the dutch general practitioners guideline: ‘headache’**

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**Background:** General practitioners play an important role in the diagnosis and treatment of migraine patients. This study aimed to

(i) evaluate the pharmacological treatment of migraine patients by general practitioners before referral to a neurologist and

(ii) to determine to what extent the Dutch College of General Practitioners (GP) guideline ‘Headache’ is used for the pharmacological treatment of migraine patients.

**Methods:** Data were collected retrospectively from 420 migraine patients (≥ 18 years of age) who consulted a neurologist for the first time in the period of January 2006 till June 2008. Diagnosis was made according the ICHD II.

**Results:** The majority of migraine patients were women (78.3%). Mean age was 39.6 (±12.04) years. Of all patients, 58.8% were diagnosed with migraine without aura, 32.6% with migraine with aura, and 8.6% with probable migraine. More than half of patients (51.7%) used triptans. Only 18.3% used prophylactic medication, although 70.2% had more than two migraine attacks per month. The majority of the patients (73.6%) had an indication for antiemetic medication. However, only 11.7% used antiemetics. Almost half of the patients (48.3%) did not reach the final step (step 3) of symptomatic treatment algorithm of the GP guideline.

**Conclusions:** Migraine specific attack medication and migraine prophylactic medication is underused in the primary care for migraine patients in the Netherlands. Almost half of the patients are undertreated, for only half of migraine patients have been treated as advised in the final step of the GP guideline ‘Headache’ before referral to a neurologist.
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